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# Arizona Medicine

JOURNAL OF ARIZONA MEDICAL ASSOCIATION

MEDICAL SOCIETY OF THE UNITED STATES AND MEXICO

Volume 18 Number 12

December, 1961

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*References:* (1) Malone, F. J., Jr.: *Mil. Med.* **125**:836, 1960. (2) Martin, W. J.; Nichols, D. R., & Cook, E. N.: *Proc. Staff Meet. Mayo Clin.* **34**:187, 1959. (3) Ullman, A.: *Delaware M. J.* **32**:97, 1960. (4) Petersdorf, R. G.; Hook, E. W.; Curtin, J. A., & Grossberg, S. E.: *Bull. Johns Hopkins Hosp.* **108**:48, 1961. (5) Jolliff, C. R.; Engelhard, W. E.; Ohlsen, J. R.; Heidrick, P. J., & Cain, J. A.: *Antibiotics & Chemother.* **10**: 694, 1960. (6) Lind, H. E.: *Am. J. Proctol.* **11**:392, 1960.

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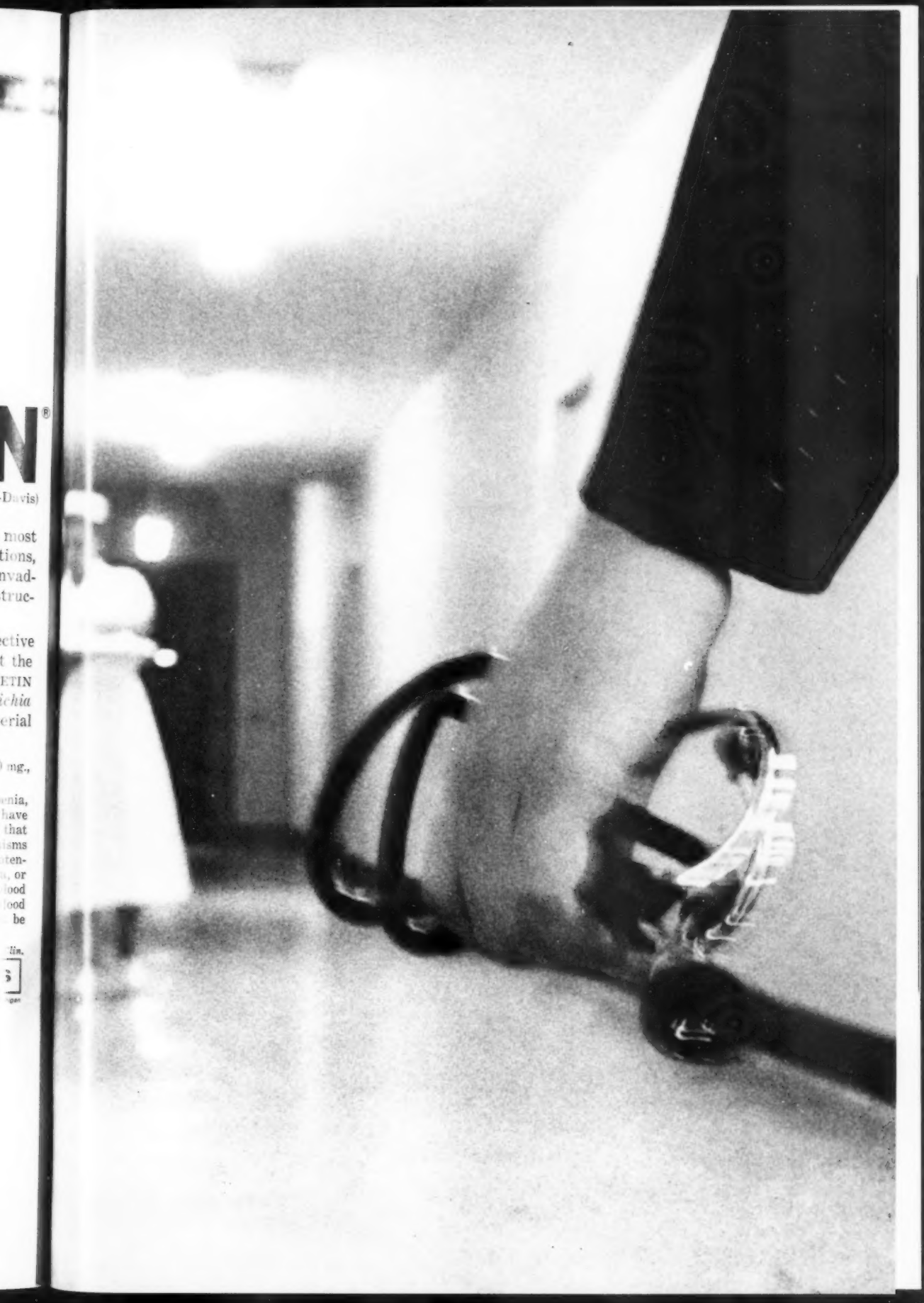

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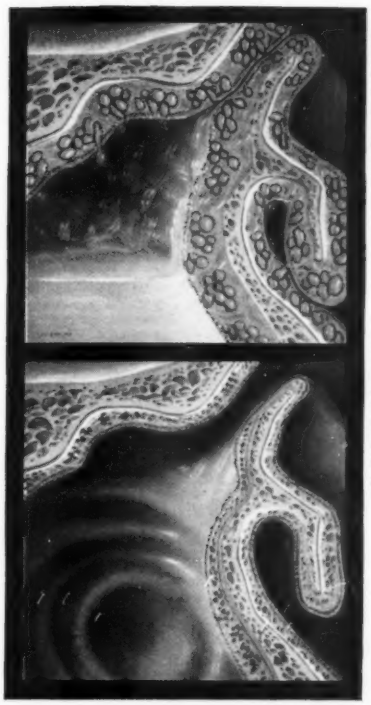

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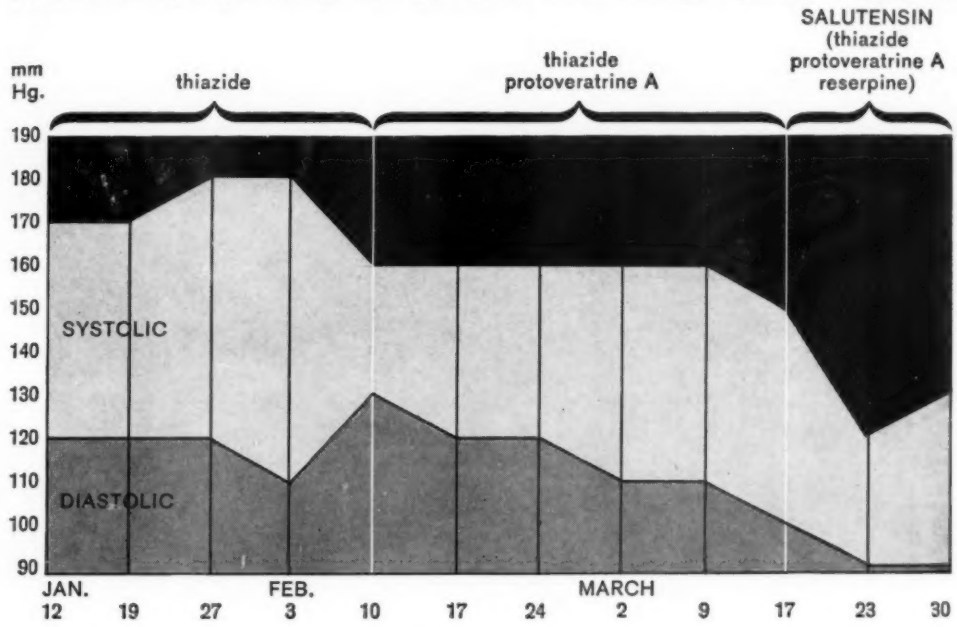
(Adapted from Spiotta, E. J.: Report to Department of Clinical Investigation, Bristol Laboratories)

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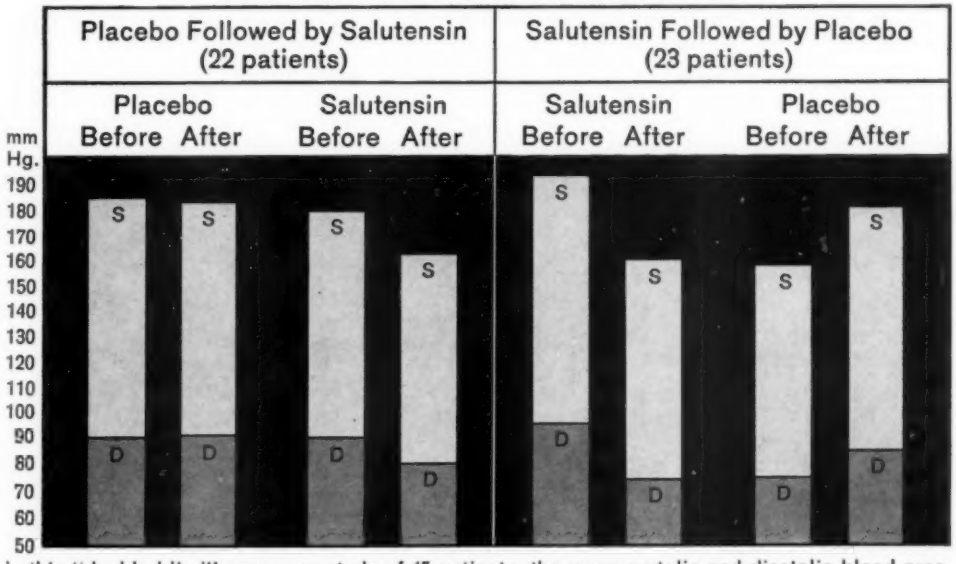


In this "double blind" crossover study of 45 patients, the mean systolic and diastolic blood pressures were essentially unchanged or rose during placebo administration, and decreased markedly during the 25 days of Salutensin therapy. (Smith, C. W.: Report to Department of Clinical Investigation, Bristol Laboratories.)

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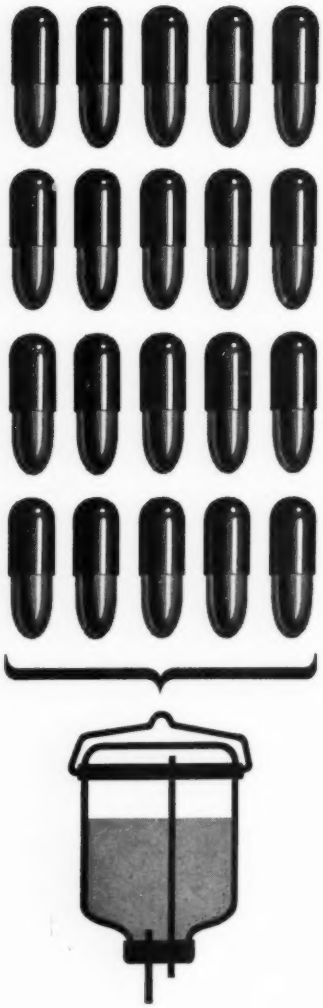

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Original Articles

Arizona Medicine

December, 1961 Vol. 18, No. 12

# Extended Operations For Alimentary Tract Malignancy: Including the Esophagus, Stomach and Colon, Together With Recital of Experiences With the Second Look Operation

Owen H. Wangensteen, M.D.

*"The silent interval in cancer is almost two years in length. We need to develop and assess methods which serve to identify patients who have cancer before symptoms become evident . . ."*

THERE IS nothing very hopeful to say yet about cancer. The best prophet of the cancer game I have encountered was King George V. He opened the first International Cancer Conference in London in 1928, and speaking through his counsellers, by one of whom the King's message was read, said: "I note with interest that your object is research, both into the cure and causes of cancer. No doubt in the last resort the discovery of the cause is the only certain and absolute means of cure. But I am glad that you have not ignored the practical side of the problem. Remembering the thousands of sufferers from cancer, I feel that if your discussions lead to advance in diagnosis, treatment, or even palliation of the disease, this Conference will have justified itself and earned the gratitude of mankind."

Many of the people, privileged to hear the King's message — almost as long ago as when Virgil Counseller and I were young surgical apprentices at the Mayo Clinic where I had the privilege of being an Exchange Surgical Fellow from the University of Minnesota in the year 1924 — believed as I did then that the King had underestimated the capacity of the assembled investigators. Many International Cancer Conferences have been held meanwhile, but those prophetic and timely words of King George V might very well have been employed to invoke any cancer conference held in the intervening years.

Strides are being made. But those of you who are surgeons and work in this area must feel at times as I have felt, we are on the wrong side of the woodpile. We would like to get over to the other side where the green cases are piling in day after day. But we fail to recognize most visceral cancers until the patient has had symptoms for some time. However much we lament the circumstance that patients may not respond immediately to the urging of a symptom, the

From the Department of Surgery, University of Minnesota Medical Center, Minneapolis 14, Minnesota.
Presented at the Phoenix Surgical Society, Phoenix, Arizona, December 15, 1960.
The researches on which this presentation is based received support from a number of sources, including the following:
Damon Runyon Memorial Fund for Cancer Research and the Minnesota Division of the American Cancer Society (Second Look Aspects of the Problem).
The American Cancer Society and the Atomic Energy Commission (P32 Studies on stomach, colon and breast)
General support from the Donald J. Cowling Fund and the J. and Rose Phillips Fund for Surgical Research.

much more important thing is that the silent interval in canver, as in cancer of the stomach and colon and in the lung, too probably is in the area of two years.

*Recruitment for Medicine*

Those of you who studied German in high school, like myself, long years ago probably read Theodor Storm's "Immense". Today, the reading of foreign languages is no longer required by many medical schools. In fact, if the applicant can read and write English and can pass his college examinations reasonably well, he probably can be admitted to a medical school, with a few explanations. Recruitment is our chief problem today in medical schools. Despite the birth rate explosion that Dr. Counseller referred to, which has not only affected Phoenix but our whole country and most countries of the world — even so not as many young men and women are studying medicine as we need. We graduate currently approximately 7,500 physicians annually in the United States. The main reason we have as many foreign physicians in our hospitals for training is that there are not enough American men and women graduating from our medical schools to man our hospitals and to fill the places available for specialty training; hence the need for continuance of a liberal policy relating to the influx of foreign physicians. Reliable sources suggest we should graduate 10,000 physicians annually to meet our current needs, let alone provide for increases in the future. Our 85 medical schools are not enough to meet this need. We are told 20 more medical schools are needed now. Phoenix could well supply one of those. In fact, in the not too distant future, the great State of Arizona certainly will have a medical school. Many medical schools, like our own, could take more students for the clinical years. If a few universities with strong science faculties could be persuaded to enter the training field in medicine for the preclinical sciences, some of the large metropolitan medical school centers could, I am very certain, absorb a larger number of students for the clinical years.

*Cancer Detection*

Theodor Storm, to whom I just alluded, died of gastric cancer. Just before he died he wrote a poem entitled, "Beginn des Endes" — the beginning of the end. The poem concerned 12 lines; in essence the thesis of the three stanzas was: I have a pain, it is nothing, and finally, it is too late. Unfortunately, this is still the way it is today with many cancers. We hope to get over to the other side of the woodpile. If presently we come to the end of the beginning, to use a Churchillian phrase, I would like to believe it will be in the area of diagnosis. However heretic it may sound to say so, I believe in 196 one could make a far more direct, immediate and important percussion upon the problem of cancer, if regularly we could detect cancer early, than if the cause of cancer were discovered. Ultimately, ascertainment of the nature of cancer and its origins, will influence greatly and favorably our fight against cancer. Implementation of such knowledge, even if available, will not be however an overnight phenomenon. Witness how long it was before discovery of the tubercle bacillus made itself felt in the mortality columns of tuberculosis.

There is a significant difference in the accomplishment in Cancer Detection Centers with a few special cancers than is achieved in the management of similar cancers recognized in symptomatic patients. As all of you know, cancer detection centers have not been too successful. There is an enormous labor involved for the dividends earned. Yet your money in the bank probably does not earn a larger percentile dividend. It was not so long ago that money in the banks earned only 1 per cent. Why should we complain, when we are dealing in human lives if only three cases are found amongst 100 patients above 45 years going through such a detection center?

Just under 20 per cent of all deaths in this country are caused by cancer. The other important causes of death are heart disease, and disease of the blood vessels, accidents, and congenital deformities. Together with cancer, these items comprise 85 per cent of all deaths. You can understand, therefore, why insurance companies fail to be as concerned over many other causes, which account for the remaining 15 per cent of deaths. It is important, as Dr. Counseller said, to lend continuing liberal support to organizations like the Arizona Division of the American Cancer Society. The effort and great interest in the cancer problem of this organization continues to alert the public to report for annual examinations. Inasmuch as the silent interval in cancer is almost two years in length, we need to develop and assess methods which

serve to identify patients who have cancer before symptoms become evident — an area in which a major break-through in the fight against cancer could achieve an immediate and telling effect.

## CANCER OF THE ESOPHAGUS

This discussion will concern largely gastric and colic cancer. I have a few things to say on cancer of the esophagus as well. This is one of the bleakest chapters in the surgery of malignancy. Cancer of the esophagus is primarily a cancer of males, about five to one. Cancer of the hypopharynx, however, is predominantly a cancer of females. Ahlbom (1936) suggested that the dysphagia observed in sideropenic anemias, accompanied by achlorhydria may be a harbinger of the development of esophageal cancer. Leukoplakia of the esophagus is probably an occasional precursor of esophageal cancer.

The success of surgeons with cancer of the esophagus, in many ways, has been disappointing. Sweet of Boston (1954), who is one of the keenest American exponents of esophageal surgery, has published results which suggest that, the operation for cancer of the lower third of the esophagus can be accomplished with a reasonable operative risk and is accompanied by a five year survival rate of 17 per cent. For curative resections, Sweet's 5 year survival rate was 34 per cent for cancer of the distal third of the esophagus. Sweet, however, is not enthusiastic over surgical attacks upon cancer of the upper two-thirds of the esophagus. Cancer of the cervical esophagus is still in its developmental stages. No surgeon yet has a brilliant record to report with this easily accessible cancer, the excision of which creates so many extremely difficult surgical problems.

It is strange indeed that squamous cell cancers of the esophagus are rather refractory to x-ray treatment, especially in the light of the circumstance that squamous cell cancers of the skin as well as of the cervix respond well to this mode of management. The nature of the difference in response is difficult to discern.

Some American surgeons, (Humphreys and Huestow) have expressed keen disappointment over their failure to achieve five year cures in their own clinics in patients with cancer of the esophagus. Whereas we have a number of five-year cures following surgery in this clinic, the over-all mortality has been such that one cannot be enthusiastic over the accomplishment. It would be nice indeed if cures could be achieved by roentgen treatment without the mortality incident to surgical therapy. Up until now, however, the achievement of the radiologist with cancer of the esophagus has not been promising.

### *The Operation for Cancer of the Esophagus*

My operation for cancer of the esophagus is conventionally a combined procedure; a mid-line upper abdominal incision with a split of the sternum into the fourth interspace. This maneuver permits easy access to the abdomen, providing an opportunity for assessment of whether or not there are subdiaphragmatic metastases.

The esophagus itself is mobilized by an incision in the third interspace. The superficial portion of the incision extends as far laterally as the latissimus dorsi mucle. However, the intercostal muscles between the third and fourth ribs are divided along the superior surface of the fourth rib along the entire length of the rib to the transverse process of the spine. The 3rd and 4th rib cartilages are divided anteriorly, and if need be to provide exposure, the second cartilage is similarly divided. The insertion of a Burford rib spreader permits ready access to the upper mediastinum. Even for cancers involving the lower portion of the thoracic esophagus, over a period of many years, I have made it routine practice to divide the vena azygos and to begin mobilization of the thoracic esophagus at this level. The merit of this procedure lies in the circumstance that, one is able thereby to excise a goodly segment of the esophagus proximal to the cancer as well as distal to it. The failure of a number of American surgeons to achieve five year survivors with partial esophagectomy is owing, I believe, to the circumstance that, the esophagus is divided too close, on the proximal side, to the cancer.

The criteria of a satisfactory cancer operation for malignancy of the esophagus are:

1. Adequate excision of the esophagus with sacrifice of normal esophagus proximally as well as gastric tissue distal to the lesion; 2. an adequate lymph node dissection; 3. a form of resti-

tution of anatomical continuity which will provide satisfactory function and will not be accompanied by a large mortality.

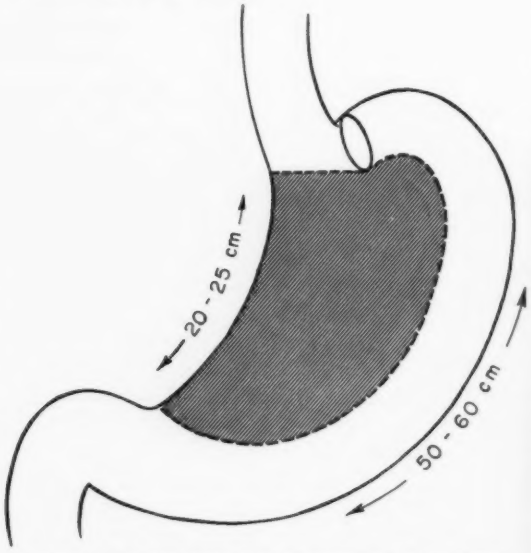


**Figure 1. The Mes gastric tube for replacement of the thoracic esophagus, following its excision for cancer. The lesser curvature of the stomach is sacrificed. A pyloroplasty is added because of the concomitant vagotomy attending excision of the esophagus.**

More and more throughout the world, surgeons affecting an attitude of interest in esophageal surgery are returning to the Franz Torek procedure of ridding the patient of his cancer at the first operation, reserving restoration of continuity to such a time that the patient can well tolerate the procedure.

The exploration described above does not provide the degree of visualization of the esophagus which can be obtained by the more conventional postero-lateral approach. It has the advantage, however, that the patient lies almost supine during the greater portion of the procedure. Moreover, after pulling the lung forward, it is not difficult to visualize the esophagus behind the lung root. Adequate hemostasis is effected by pre-placement of silver clips upon the intercostal arteries before they are divided. In this dissection too, it is possible to visualize the lymph nodes and to remove them with the esophagus.

*Restoration of Continuity*

The question of restitution of continuity is today probably the most difficult problem facing the surgeon. Many like myself have continued, even with many misgivings, to employ the stomach for the purpose. The only good thing to h said for the stomach, on this score, is its avail bility. It is handy. Attachment of the stomach t the esophagus invites esophageal erosion an esophagitis. In fact, severe hemorrhage and eve perforation have been observed following elev tion of the stomach for the purpose.

**Figure 2a. X-ray film of a high-lying cancer of the thoracic esophagus.**

Mes (1948) of Capetown described a method of mobilizing a tube from the greater curvature of the stomach, a method which this writer has used with advantage in some cases. However, too, it is not free from the objections raised to use of the whole stomach. Such a Mes tube can be implanted either behind the sternum or subcutaneously. In the latter location, it is not as unsightly as placement of a segment of intact stomach beneath the skin. I have had a few successes with this method. In Figure 1 is to be seen a variant of the Mes technique which I have used for cancers of the mid or upper thoracic esophagus. By saving the distal few centimeters of the esophagus it is possible to effect the anastomosis. In such a manner that the esophagogastric juncture and sphincter are retained, thereby avoiding the threat to esophagitis occasioned by the reflux of acid pepti

juice, when a direct esophago-gastric anastomosis is made.

Because of the problems inherent in use of the stomach as a substitute for the esophagus a number of surgeons have elected to transplant the colon for the purpose of restoring esophago-gastric continuity. Petrov (1959) (of Moscow) mobilizes the cecum and brings it or the ileum, granted its blood supply can be preserved, to the divided upper esophagus. More and more, however, surgeons are beginning to use the left colon for the purpose, bringing the sigmoid colon up in an antiperistaltic fashion pedicled on the mid-colic artery. The marginal vessels along the mesenteric edge of the bowel, if undamaged, assure an adequate circulation. The transverse colon is divided proximally. The distal segment is anastomosed to the stomach and colic continuity is re-established by anastomosing the divided proximal segment of the transverse colon to the distal segment of the pelvic colon. Whereas the magnitude of the operation is greater, than migration of the stomach, the procedure is not accompanied by the untoward results so frequent after anastomosis of the stomach to the esophagus.

**Figure 2b. The situation five years after replacement of the esophagus with a Mes tube drawn up through the esophageal hiatus. The anastomosis was made in the neck, at the level of the cricoid cartilage.**

**Such tubes can be drawn up, as here, in the natural position of the esophagus, or retrosternally, or even subcutaneously. Such a tube placed subcutaneously does not leave the patient with a deformity that is very objectionable.**

It is my impression, however, that however desirable use of the patient's own tubular tissues are for re-placement of the esophagus, the very magnitude of the undertaking indicates that if a simpler method were available it would be good to employ it. Over a period of many months, my associates and I have toyed with the idea of constituting an esophageal tube from a plastic substance, using a tube fashioned from dacron, marlex or teflon into the interstices of which the tissues of the patient would grow. In the experimental animal, we implanted such tubes several weeks before their attachment to the stomach or the esophagus was effected. Unfortunately, however, the porosity of these tubes is such that the patient's own tissues which have grown into the interstices of the plastic tube are digested by the digestive juices.

More recently, we have employed a teflon tube with a large bore which is non-porous throughout the greater portion of its length. There is a short external porous over-lay at the distal end of the tube, which is sutured to the gastric wall and inverted into the stomach. Similarly there is also a porous in-lay at the proximal end into which the divided proximal esophagus is inserted. Both proximal and distal ends of the non-porous tube have a dacron apron which is used to cover the anastomosis. Whereas the method has yet not been employed in man, the utility of the method appears to have been demonstrated in the laboratory in experiments upon dogs.

## CANCER OF THE STOMACH

In cancer of the rectum and the colon the frequent precursor is very likely an adenomatous polyp. In the stomach, on the contrary, the polyp is an antecedent of gastric cancer. For most cancers of the stomach we do not know what the antecedent is. In our cancer detection center we have employed the presence of achlorhydria to histamine as a screening test for gastric cancer since the beginnings of this activity at the Univeristy of Minnesota 14 years ago. Whereas we have not much to record on the score of finding early gastric cancer, the plan has been successful in uncovering a large number of patients harboring silent gastric polyps. As Brunn and Pearl (1926) pointed out such polyps occur only

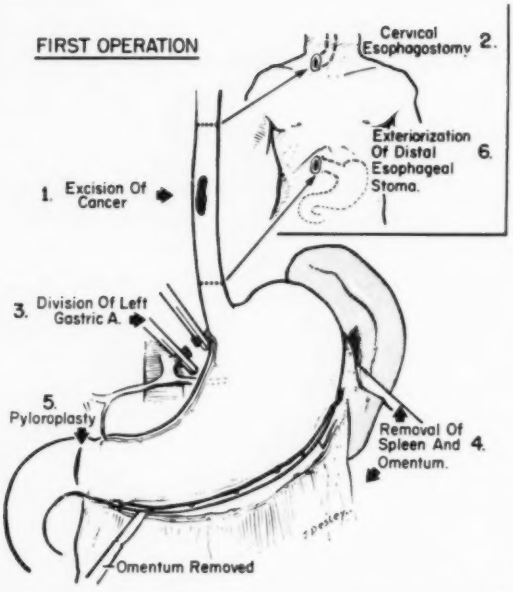


**Figure 3. Author's operation for cancer of the upper thoracic esophagus with preservation of the esophagogastric juncture, to preclude reflux of gastric juice.**

**The operation is divided into stages. In the first operation, the thoracic esophagus is excised, save for preservation of a short segment in juxtaposition to the stomach. Before the continuity is effected in the second delayed operation, the esophagostomy is brought out beneath the costal margin; experience has shown it to be an effective deterrent to leakage of gastric juice.**

in achlorhydric stomachs. Patients observed to have achlorhydria are subjected to follow-up studies with x-rays and gastroscopic examinations. Lyle Hay of this clinic has previously reported the experience of this clinic with gastric adenomatous polyps.(5,6). They are slow but definite precursors of gastric cancer. We do not excise the stomach willy-nilly when a polyp is detected, but continue to watch the patient at yearly intervals. When the polyp begins to increase in size, operation is advised, as it always is for large gastric polyps. In this way, many patients have been permitted to retain their stomachs for many years, before ultimately sacrificing a goodly segment of it in an attempt to thwart the occurrence of cancer.

*The Importance of Achlorhydria*

My humble role as a gastric consultant has usually been to ask the patient "Has your stomach been pumped?" It is extraordinary how many times the patient will have undergone numerous x-ray examinations, been gastroscoped a number of times, without having had his stomach pumped. Let me tell you of such an instance. A jurist of 50 years in my area had epigastric pain for which he consulted his physicians who took him to a roentgenologist who told him he had a duodenal ulcer. When his pain was unrelieved by the administration of alkalies and a Sippy diet, our patient asked for additional consultation. His physician took him to an internist who told him he had coronary disease on the basis of electrocardiographic findings. When neither nitroglycerin nor soda, each of which the patient carried in opposite vest pockets, did him no good, he asked for additional consultation. That is how I got into the picture. My question was: "Has your stomach been pumped?" the answer, "NO." He was found to be achlorhydric to histamine. Our roentgenologist, Dr. Leo Rigler, one of the best in the game, examined our patient with care, but with negative findings. I then told Dr. Rigler that the patient was achlorhydric. Dr. Rigler restudied the patient again with no findings. Because of pain and achlorhydria I asked Dr. Ragnar Ylvisaker to have a look. On gastroscopic examination he described a palm-sized lesion occupying the entire mid-segment of the stomach. At my request, Dr. Rigler did a third examination, and believed he could see something on the lesser curvature in the patient's gastric films. It is not often one gets a second let alone a third chance in this life. At operation, nothing abnormal in the stomach could be seen nor felt, but mindful of the gastroscopist's report, I did a 95 per cent distal gastrectomy. This patient is case No. 14 in the American Cancer Society

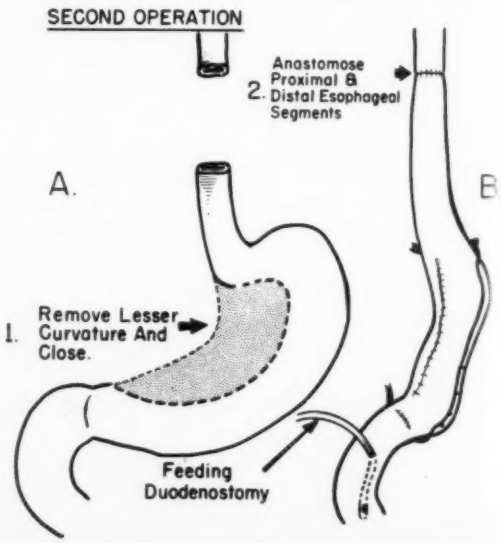


**Figure 3b. The situation after restoration of continuity.**

Monograph Series.(12) This man is alive and well today, more than 12 years later. He owes his life to the diagnostic help the achlorhydria afforded in pursuing the nature and cause of his pain. Incidentally, his coronary disease disappeared with the cancer. While some internists continue to debate whether it is worthwhile to do gastric expressions, my suggestion to you is that while our metaphysical friends engage in these unrewarding discussions, you and I go ahead and ascertain whether or no the patient's stomach is capable of secreting HCl under the influence of a stimulus such as histamine. Unfortunately, not all patients with gastric cancer are achlorhydric. In our experience approximately 80 per cent are.

This discussion should in no wise be interpreted as disparagement of x-rays in the recognition of gastric cancer. Roentgenology is still the most useful of all techniques in recognizing gastric cancer, but roentgen diagnosis of gastric cancer, obviously, has its limitations. And it is important to be alert to the shortcomings of diagnostic methods. We need to search for other methods which will complement the ability of roentgen techniques.

*Use of $P^{32}$ in Cancer Detection*

When George Moore, the Director of the Roswell Park Memorial – and may I say he has breathed the spirit of life into that institution almost single-handedly over the period of eight years he has been there – when he was one of my surgical interns in 1947 he described the special affinity between fluorescein and brain tumors. After this striking success, he and a succession of other Surgical Fellows at our institution continued the search for other similar affinities but failed to find any. Professor Komei Nakayama of Chiba City, Japan, visited us in September, 1955, and told us of his observations with a Geiger counter using radioactive phosphorus in the detection of esophageal and gastric cancer. Employing Nakayama's methods, Shahon, of our clinic, failed to find it of any real help to us in the recognition of cancers at these sites. Shahon continued his observations administering 500 microcuries of phosphorus ($P^{32}$) intravenously to patients with known cancer in the alimentary tract. In order to permit delayed histological examination of the excised specimen he covered it with Saran wrap and put in in the icebox, placing the preparation in direct contact with an x-ray film. Shahon found that after six hours exposure, the cancer could be identified as a darkened area on the x-ray film. It was obvious, therefore, that if a method could be evolved of exposing the intact stomach to a film for a period of hours, we probably could re-duplicate *in vivo* what was obviously a very helpful technique *in vitro*. At the time, we were working with gastric balloons and local gastric cooling for massive gastric hemorrhage. It was natural, therefore, to identify a gastric balloon with the requirements of the situation and thus the technique I shall now describe in the recognition of gastric cancer was born.

The patient is taken to a dark room where he swallows the balloon (condom) which has been coated with a photosensitive emulsion, developed by Eastman Kodak Company. The patient is given intravenously 500 microcuries of $P^{32}$ 24 hours before he swallows the balloon. The patient returns to the ward and comes back to the dark room six hours later for extubation.

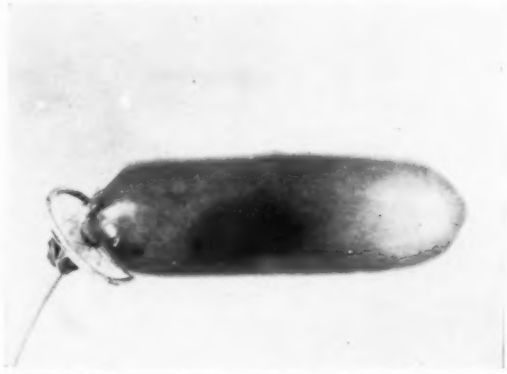

**Figure 4. Preoperative radioautograph of a gastric cancer. The patient had been injected with 500 microcuries of P32. The black area indicates the site of the cancer, which was verified by operation.**

A developing solution is poured into the balloon. The result can be read almost immediately. A dark area on the balloon suggests the presence of a cancer. Whereas George Moore dealt with disparity differences of 8000 per cent (greater uptake of fluorescein by brain tumors as contrasted with the contiguous normal tissue), the differences in absorption of $P^{32}$ by cancer and the adjacent normal tissue on the contrary is slight, being only of the order of 50 to 100 per cent greater by the cancer. However, amplification of this small difference by the element of time over a period of six hours makes an important difference. My colleagues, Drs. Norman

Ackerman and Arthur McFee, and I are inclined to believe that this method will become a valuable complement to other methods in the recognition of gastric cancer. Unlike the x-rays, its worth is contingent solely on the slightly greater affinity of the cancer for phosphorus as contrasted with the normal contiguous tissues. Rarely do roentgenologists recognize mucosal gastric cancer. Usually it is only when the cancer invades the gastric wall and interrupts normal gastric peristalsis that the roentgenologist is able to make the diagnosis.

A few benign gastric ulcers have been erroneously identified as gastric cancer by this technique which is not a serious error. A more disturbing occurrence is that two gastric cancers were not recognized by the method. Yet, the method would appear to have an index of accuracy in the identification of gastric cancer at least comparable to that of roentgenography in expert and experienced hands.

Currently we are exploring use of $P^{32}$ in the detection of tumors of the breast(6a). The method in established clinical cases of breast cancer apparently is working out as well as it has in the stomach. We are proposing presently to begin screening patients for breast cancer by this method in our Cancer Detection Center.

It should be possible, of course, to do multiple organ screening simultaneously. We are hopeful, in addition to the stomach, in females we may be able to do the breast and cervix too. Molds are being developed for these various anatomical sites. We are working too with a long sausage-like condom casing in the colon, hopeful that the method may be useful there as in the stomach, though obviously the technique of getting the colon balloon down to its ultimately desired location may always be a bit of a problem. Employing protoscopic techniques, we are currently exploring the promise of the method in areas of the colon beyond the reach of the sigmoidoscope.

*Treatment of Gastric Cancer*

The only treatment of gastric cancer is surgical removal. A ventrical upper mid line incision with an added extra pleural split into the fourth intercostal space, together with cutting diaphragmatic mid line fibres down to the serous pericardium provides excellent exposure. With the sternal costal arch divided and the fibrous pericardium slit, the last restraint to traction is gone.(12) This maneuver simplifies considerably the task of the person holding the retractor.

For large cancers along the lesser curvature of the stomach it is wise to do total gastrectomy, lest residual cancer be left at the site of section at the esophagogastric juncture. Total gastrectomy does *not* make digestive cripples, as some have insisted.

If surgeons making gastric reservoirs would devote the same energy in impressing upon the patient the necessity of eating, he might find far less indication for making gastric reservoirs. While the patient is still in the hospital my associates and I urge frequently upon the patient the importance of this instruction relating to food ingestion. Following operation patients with total gastrectomy are seen regularly in the Out-Patient Clinic, at two or three week intervals. The patient is urged to drink milk as a source of protein. If the patient's weight declines and edema comes into evidence, he is warned that he will be hospitalized in a couple of weeks if the record does not look better on the next visit. If the patient returns with ankle edema, he is admitted to hospital, a No. 18 large red rubber, four-hole duodenal tube is inserted into the nose through which whole milk is dripped constantly day and night. Three to four quarts of milk are given daily by this method. After about four days, or even less, the patient invariably says "Uncle" and from then on there is no further trouble with eating. This is my substitute for a man made gastric reservoir and the method has worked extremely well over a period of more than a dozen years. In other words, the patient has made the very important transition from rejection to acceptance.

My colleagues and I thought we were doing a reasonably radical operation for gastric cancer until the studies of Arhelger in my clinic, on second-look residuals, showed very definitely that residual cancer, not infrequently, was left by the surgeon in the primary operation in lymph nodes along the hepatic pedicle going to the liver and behind the first and second portion of the duodenum. Since Arhelger's (2,3) studies, we have added dissection of these areas as a regular component of the primary operation.

The two components of a satisfactory cancer operation are: 1. adequate excision of the organ involved, 2. satisfactory lymph node removal. For a large number of gastric cancers, an extensive subtotal excision, accompanied by an adequate lymph node dissection, suffices. In performing total gastrectomy, I have reverted to the technique of anastomosing esophagus and jejunum which I described more than a decade ago (1949).(10) The placement of the sutures beginning at the mesenteric border affords the surgeon the opportunity to make a secure posterior buttress, which provides protection against leakage. A generous enteroanastomosis is added also. Obviously, a Roux Y anastomosis would protect even better against retrojection of bile into the esophagus. However, the procedure described herein can be done at an operative risk about the same as that of subtotal excision, (less than five per cent) whereas the Roux Y operation in my hands commanded a 10 per cent mortality. The way to have a reasonably good record of ultimate survivors is to have as many survivors from an adequate operation as possible.

In our clinic, since 1936, there have been 188 patients who have survived five years or more. A large number of these have lived ten years and several 15, and a few even 20 years. This record, to be certain, is a very modest one, but there is no room for therapeutic Nihilism in gastric cancer.

## CANCER OF THE COLON

Approximately 75 per cent of cancers of the large bowel (colon and rectum) are within reach of a 25 cm. sigmiodscope. The shortcoming of the endoscopic procedures in the large bowel is distance — inability to visualize the more proximal reaches of the colon.

### *Near Total or Total Colectomy for Colic Cancer*

For a number of years I have championed total or near total colectomy as the primary operation for all colic cancers distal to the hepatic flexure.(11) It is surprising how often an unexpected cancer is found in the excised colon in an area which is not reached by the conventional segmental colectomy. Moreover, eventuate in cancer, are encountered frequently when near or total colectomy is done for colic cancer.

For cancer of the colon proximal to the hepatic flexure, in which instances, excision of terminal silent adenomatous polyps, which probably ileum is necessary to catch the lymphatic drain-

**Figure 5. The extent of the lymph node dissection in gastric cancer. In this picture, total gastrectomy is depicted with restoration of continuity by a Roux Y anastomosis. In recent years, this writer has returned to end-to-side esophagojejunostomy, described previously (1949), because of the lesser operative risk attending performance of the procedure. A generous enteroanastomosis is also provided.**

**The Roux Y technique of anastomosis does afford complete protection against reflux. If the esophagojejunostomy is followed by bothersome esophagitis, at a subsequent second-look procedure, the afferent jejunal loop is divided, thus gaining the protection against regurgitant esophagitis provided by the Roux Y procedure.**

age area in the operation, excision of all the distal colon would deprive the patient of his colic reservoir which consideration is unimportant in the patient who retains his ileum.

The technique of anastomosis employed in this clinic for a quarter of a century has been and continues to be a closed operation. We conveniently give no antibiotics prior to operation — only cleansing enemas. Before the anterior row of sutures is tied, the posterior row is injected from within. Frequently a few interrupted sutures of catgut are placed in the posterior row from within, to provide a secure mucosal closure posteriorly. The instruments used in this portion of the procedure are discarded and the surgeon dons a new pair of gloves.

The primary operative mortality for colectomy in this clinic continues to be between 4 and 5

per cent. For Dukes Group A lesions, the 5 year survival has been in the area of 80 per cent; for Dukes B lesions about 65 per cent; the Dukes C lesions, with lymph node involvement the 5 year survival has been 45 per cent.

*The Second Look Program*

It was the large disparity in accomplishment between lymph node negative and positive cancers that suggested the need for the Second Look Procedure.(11) Obviously, the second-look program makes it mandatory to tell patients they have cancer. I have yet to surprise a patient by telling him he has cancer. He knew it before.

The areas in which the second-look procedure has demonstrated its worth most effectively are: 1. cancer of the colon; 2. retroperitoneal fibrolipomyxoma sarcomas, currently described as rhabdomyoscarcomas; 3. the ovary.

The second-look procedure is undertaken conveniently six months after the primary operation. The patient is re-explored at similar intervals until either the cancer gets out of hand or the patient becomes cancer negative. Four colon cancers have been converted through this procedure to become cancer negative and survive for long periods of time up to more than ten years. Of eight retroperitoneal fibrosarcomas, three have been converted through use of the second-look procedure. These are enormous tumors and it is not unusual, I believe, to find on second entry in asymptomatic patients a few residuals from the first procedure.

In cancer of the ovary with evidence of carcinosis, four out of 22 patients have been converted. This is an area for use of the procedure which demands wider attention and approval.

The overall salvage rate in the areas in which the second-look procedure has been employed is 10 per cent, a small accomplishment to be sure. However, this concerns patients who would have succumbed to their malignancy without repetitive surgical intervention. Is this small accomplishment worthwhile? Ask anyone who has had cancer residuals and been converted to a cancer free state.

*Summary*

Over the past three decades, slow but definite progress has been made by the medical profession in its fight against cancer. The hope of the future lies in earlier detection. The ultimate solution of the cancer problem will come only when the nature of cancer is understood and when we have learned to prevent it. Long before that day, however, specific organ scrutiny tests will undoubtedly have been found for many of the frequent visceral cancers. In fact, techniques which will permit recognition of cancer in the long asymptomatic, silent interval, will make a tremendous impact upon the cancer problem. That day is now probably not far away.

The experience of this clinic with cancer of the esophagus, stomach and colon has been reviewed. A technique of excision of the upper thoracic esophagus with preservation of the esophago-gastric juncture, employing a Mes-type of gastric tube has been described.

The second-look procedure has been found particularly useful in the colon, and for large retroperitoneal rhabdomyosarcomas and for cancer of the ovary. An overall ten per cent conversion rate has been achived in these otherwise hopeless cancers — a modest accomplishment to be sure, but how otherwise could those patients have been cured today? Moreover, even when second-look procedures fail to effect lasting conversions to a cancer-free state, surprising prolongation of life is often achieved.

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# The Pathology of Ruptured Ventricle

Ian Stewart, M.D.

*A review of 29 coroner's autopsies shows rupture of the left ventricle not only to occur in areas of fresh or healed myocardial infarction (17 cases), but also in fatty infiltration of the heart (7 cases), arterial hypertension (3 cases), aortic stenosis (1 case), and without evident cause (1 case).*

THE RECENT articles by Crawford and Morris (1960) and Mitchell and Parish (1960) were devoted almost exclusively to statistical details of ruptures of the ventricles obtained respectively in London, and in Oxford and Birmingham. Crawford and Morris, under the heading "Pathological Findings" say, "At necropsy pathological evidence of hypertension was very commonly noted and a history of diabetes frequently mentioned but because of the nature of these deaths there are no reliable data on blood pressure and associated conditions during life (likewise retrospective social analysis proved impracticable)." After quoting the sites of rupture they conclude, "Very severe coronary atheroma and coronary occlusion were usually reported."

Mitchel and Parish open their article with the words, "Rupture of the heart is a dramatic complication of myocardial infarction . . . " and this provides the keynote of their analysis of the 46 cardiac ruptures which occurred in the Radcliffe Hospital, Oxford and in the Queen Elizabeth and General Hospitals, Birmingham from 1939 to 1959. It is natural that patients who suffer a cardiac infarct and survive long enough to be observed closely in the ward and hospital mortuary should provide the material for their figures. They furnish also details of the cases of rupture which were the subject of a coroner's enquiry in the City of Birmingham for 1951-60, 25 in all, but do not give details of the pathological findings in these cases. One is left with the impression after reading both papers that ventricular rupture is the sequel to cardiac infarction and to no other condition.

This paper gives details of the necropsy findings in 29 cases of spontaneous ventricular rupture I have examined in the Craven District of Yorkshire in the years 1953-60. These were all cases within the Coroner's purview. None of them occurred in hospital and none of them had been in medical care. As will be seen a variety of conditions, sometimes in combination, were responsible for the disaster.

A. *Fatty infiltration of the Heart (7):* These were cases in which there was a great excess of epicardial fat which was accompanied by visible fatty penetration of the myocardium. The coronary arteries were normally patent with opaque walls showing varying amounts of fatty change or calcification. No sign of coronary thrombosis was found and there was an absence of the signs of recent infarction, that is of hyaline pallor, at the site of rupture. The ages of the persons were as follows:

Man: 63
Women: 66, 67, 68, 76, 78, 80.

The site of rupture in five women was in each case the anterior wall of the left ventricle just above the apex. In the sixth woman the rupture was midway along the left border of the heart. In the man the site of rupture could not be distinguished and must have been extremely small: the layer of fat on the anterior surface of the

Consultant Pathologist, Keighley.

heart was separated from the muscle by a ¼ inch thickness of clot and the pericardium was distended by blood and clot. Six of them showed no fibrosis of the myocardium. In one of the women rupture had occurred along the margin of a fibrotic patch.

B. *Arterial Hypertension (3):* In these cases these was marked ventricular hypertrophy, widely patent coronary arteries in two of them and only a moderate narrowing of the left vessel in the third. There were no signs of fibrosis or of infarction or of excess epicardial fat.

Ages: Man: 72 (heart weight 15 oz.)
Woman: 71 and 79 (Heart weights 16½ oz. and 17½ oz.)

The ruptures in one man and one woman were on the left border of the left ventricle and in the other woman in the lower anterior wall of the left ventricle.

C. *Myocardial Fibrosis with coronary obstruction (2):* A woman of 69 years with tortuous calcified coronary arteries which showed obstruction. The posterior wall of the left ventricle in an area 1½ inches in diameter was thin and fibrotic and rupture had occurred in its centre. The man, 82 years old, had calcified coronaries, the right being moderately narrowed and the left severely. There was a fibrotic thickening of the lower half of the front wall of the ventricle with rupture through its centre. There was no evidence of a new infarction but as the myocardium was largely absent in the fibrotic zones it would be most difficult to diagnose or deny.

D. *Coronary Thrombosis with fresh infarction (4):* these were all women. The coronary arteries showed varying degrees of advanced atheroma. None of them showed ventricular hypertrophy, excess epicardial fat or previous fibrosis.

Their ages were: 69, 75, 76 and 84.

In two the thrombosis was in the right coronary and the infarct and rupture in the middle of the posterior wall of the left ventricle. In the others the thrombosis was in the descending branch of the left vessel, with anterior rupture just above the apex in one and in the middle of the left border in the other.

E. *Coronary occlusion with infarction ( ):* These again showed no ventricular hypertrophy, excess fat or previous fibrosis. The left coronary in each was almost closed by calcification or fatty change and there were varying degrees of obstruction in the right vessel. No thrombi were found.

Ages: Men: 68, 73.
Women: 72, 72, 74, 79.

In five the rupture was in the zone above the apex on the anterior wall of the left ventricle and in the sixth near the upper end of the left border. In one woman the rupture was limited to the outer half of the myocardium and did not penetrate into the ventricle.

F. *Myocardial fibrosis with Coronary Thrombosis (2):* Both were women with thrombosis in the left vessel. In each the lower front wall of the left ventricle was almost wholly fibrotic and rupture had occurred through the centre of the zone.

Ages: 74 and 87.

G. *Infarct without obstruction (2):* Both had large fresh infarcts of the middle of the posterior wall of the left ventricle and rupture in the centre of these. Both coronary vessels were patent in each case.

Ages: Man: 54 Woman: 73.

H. *Rupture without evident cause (1):* A man of 78 in whom the coronary arteries were calcified and only slightly narrowed. There was no thrombus, no ventricular fibrosis, no ventricular hypertrophy and no excess of fat. The myocardium was of normal appearance. On the back of the left ventricle close to the septum was a vertical split one inch long.

I. *Hypertension with infarction (1):* A man of 71 in whom the heart weighed 20 oz. The right coronary was almost blocked by a signet ring fatty patch 4 inches from its origin. A fresh infarct in the lower half of the septum had ruptured into the right ventricle. This case is

usual in that the man died abruptly. As Crawford and Morris have pointed out, death in septal rupture is usually delayed.

. *Aortic stenosis (1):* A woman of 84 with a massively calcified bayonet shaped aortic valve. The coronary vessels were widely patent and partly calcified. There was no thrombosis and no visible infarct. There was a ragged tear in the middle of the back of the left ventricle.

*Discussion:* It will be seen from this list that the elements which singly or in combination enter into the causation of ventricular rupture are slow coronary occlusion, abrupt thrombosis, arterial hypertension, myocardial fibrosis, fatty infiltration and myocardial infarction. Rupture may even occur in the apparent absence of these factors. Crawford and Morris, in comparing hospital cases with those in the Coroners records state "how unrepresentative the post mortem material of teaching hospitals, the source of most statements on morbid anatomy, may be." The cases produced here are certainly different from the hospital cases quoted by Mitchell and Parish, which were all known cases of myocardial infarction. The latter authors observe that the sex ratio in rupture of the heart differs from that in myocardial infarction and quote several authorities who had also noted this. This discrepancy seems likely to be due to the assumption that rupture is due only to infarction. The cases described here suggest that fatty infiltration, hypertension and other factors have not been given the consideration they deserve.

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# Arizona Workmen's Compensation Law As It Applies To The Practice Of Medicine And Surgery

**Walter V. Edwards, M.D.**

*Dr. Edward's paper is a very helpful presentation and acquaints us with some of the history of the Workmen's Compensation Law and its application to the practice of medicine in Arizona. The contents of this paper should be helpful to all practitioners since almost all doctors are called upon to treat industrial accidents. A background of the compensation law and the manner in which it operates should therefore be well worth reading by all Arizona practitioners. An occasional article of this type should keep us abreast of the Workmen's Compensation Law and its application to the practice of medicine and surgery in Arizona.*

INTRODUCTION: It is a distinct privilege and honor to be permitted to appear before you, my peers in the field of orthopedics, after a somewhat checkered career in the fields of medicine and community activity. Several months on the orthopedic service of a station hospital during World War II handling sprained ankles and disposition back and foot problems do not qualify me to discuss orthopedic problems specifically, nor does several months of handling battle casualties make me an expert in the field of trauma. Nine years of general practice in a rural area with a professional emphasis placed on obstetrics do not make my appearance before you entirely appropriate. However, during the latter years of general practice, one term spent as a Representative to the State Legislature from Yavapai County developed in me an interest in the law and in its application to our personal and professional lives. A subsequent five years spent in employment at the Arizona State Hospital dabbling in geriatrics and psychiatry as well as general medicine and surgery, provided opportunity for informal training in emotional disturbances and in administrative procedures, and under the guidance of Tiny Tuveson, I did set a few bones. The sequence of events lead to my association approximately eight months ago with your colleague, "Gentleman Jim" Moore.

In the course of functioning as assistant to Dr. Moore during these months I have been privileged to be in frequent contact with many of you and to have discussed, both formally and informally, a number of things which I wish to discuss with you this evening. The idea of such discussion was brought up to me some time ago by Tom Taber and John Ricker. With relative inexperience in the number of fields previously mentioned, I do not come before you with any great message or any startling observations. However, through the months I have made mental notes, as well as some written, of a number of problems related to the management of industrial injuries and diseases, both from a professional as well as from an administrative point of view. I trust that Dr. Moore, and others among you who have had more experience than

Presented at the meeting of the Arizona Chapter, Western Orthopedic Association, Ho Ho Kam Country Club, Coolidge, Arizona, February 24, 1961.

I will be patient with me and will correct me gently. Criticisms, questions and discussion from the floor will be most welcome, as time permits, when I conclude.

HISTORY: In order to better understand the nature of the problems with which we deal, we must be aware of some of the history of the Workmen's Compensation Law. Prior to the recognition of the statehood of Arizona, the injured workman, in the event of incapacitating injury occurring in the course of or as a result of his employment, had no recourse against his employer except through the courts. Before the days of many safety features in the mines, serious industrial injuries were common enough and were catastrophic to the injured workman. An enlightened constitutional convention wrote into the constitution a provision that – "The legislature shall enact a workmen's compulsory compensation law applicable to workmen engaged in manual or mechanical labor in such employments as the legislature may determine to be especially dangerous, by which compulsory compensation shall be required to be paid to any such workman by his employer, if in the course of such employment personal injury to any such workman from any accident arising out of, and in the course of, such employment is caused in whole, or in part, or is contributed to, by unnecessary risk or danger of such employment, or a necessary risk or danger inherent in the nature thereof, or by failure of such employer or any of his or its officers, agents, or employee, or employees, to exercise due care, or to comply with any law affecting such employment; provided that it shall be optional with said employee to settle for such compensation, or to retain the right to sue said employer as provided by this constitution." The wording of the constitutional provision and subsequent statutes resulted in inadequate protection of the injured workman because of the need for litigation in many cases to determine the employer's liability and the amount of compensation for the injuries sustained.

In 1925 a constitutional amendment was passed by the people to obtain a release of the injured workman and his family from burdensome and expensive litigious remedies for injuries, death and the uncertain and unequal compensation provided under the old law. The latter constitutional amendment, however, also provided that *percentages and amounts of compensation provided should never be reduced* nor any occupation eliminated except by further constitutional amendment. Since the effective date of this amendment and subsequent statutes, the injured workman has been much better protected. In fact, through liberal interpretation of the law by the courts a percentage of workmen are pampered and are castrated of motivation.

THE INDUSTRIAL COMMISSION: As most of you are aware, the Industrial Commission is composed of three members appointed by the Governor with the advice and consent of the State Senate. Each member is appointed for a six-year term with the expiration of terms staggered every two years. No more than two of the three members shall be of the same political party. The duties of the Industrial Commission are many, but include most specifically the administration of the Workmen's Compensation Law, the underwriting of workmen's compensation insurance, the classification of employment categories, the promotion of voluntary arbitration, mediation and correlation of disputes between employers and employees, the licensing and supervision of the work of private employment offices, the accumulation and collating of statistical information regarding employment, etc. The Commission holds a quasi-judicial status, and appeal of the decisions of the Commission are made directly to the State Supreme Court.

THE INDUSTRIAL COMMISSION AND THE DOCTORS: As citizens and residents of the State of Arizona and, as doctors of medicine and surgery licensed under the laws of the state, we are obligated to uphold the provisions of the Workmen's Compensation Law. As so licensed, we are authorized to provide care for the industrially sick and injured. In so doing, however, we are also obligated to function in accordance with the rules and regulations of the Industrial Commission. This is no thesis for the socialization of medical practice, but to be realistic we must recognize the entry of a third part into the patient-doctor relationship in our handling of industrial patients. As a matter of policy, the Industrial Commission has, however, done all in its power to maintain the patient-doctor relationship and at the same time to provide the injured

workman with the quality and quantity of care to which he is entitled under the law as it is written. We may have our dissatisfactions with many real or imagined problems in the area of industrial medicine. However, as you are fully aware the Industrial Commission has worked closely with the medical profession through the Industrial Relations Committee of the State Medical Association and has used the same body as a Medical Advisory Board which, to the Commission, is the medical supreme court within the state. Through the Industrial Relations Committee many problems have been at least partially solved, such as the Medical and Surgical Fee Schedule and the Rules and Regulations applicable to doctors handling industrial problems.

PROFESSIONAL RESPONSIBILITY TO THE INJURED WORKMEN: Among a number of things the law requires that the physician who sees a patient with an injury or an illness which, in the opinion of either the injured workman or the doctor, may reasonably be related to his employment, shall assist the workman in filling out and filing the proper forms. The filing of such forms, however, does not necessarily qualify the case for benefits under the Workmen's Compensation Law. When the doctor's report of injury, the employee's report, and the employer's report have been received by the Industrial Commission, the case may then be legally accepted as an industrial responsibility by the Commission under the law on the basis of the information provided. In the majority of cases where an individual receives a laceration or a fracture in an accident incurred while working, there is little question as to the industrial responsibility in the case. However, when a patient claims an injury and delays a week or a month before reporting to a physician with a problem which may be as much due to arthritis, for example, as to an alleged injury, the industrial responsibility is open to question. The statement of the physician that, in his opinion, the problem is related to the injury alone is not enough. In filing his report the doctor should state specifically, rather than imply, the relationship of the patient's problem at the time he is seen to the alleged injury. Without such analysis the Commission is not in a position to accept the case. The forms are, of course, filed with the Claims Department and if they are in doubt as to the relationship, the file is usually referred to the Medical Advisor for review. If the rela tionship is not clear to the Medical Adviso with the statements at hand, further informatio from the attending physician is sought until th relationship is more clear. If the attending phy sician continues to report only an opinion, i order to clarify the situation from a medical-l gal point of view, the Commission is then in position to ask for a group consultation usuall using the attending physician, appropriate sp cialists and the Medical Advisor. The need fo such consultations, however, can be obviated a most completely by an adequate history-taking, clinical study and reporting by the attending physician.

Because of the almost necessary bureaucratic delay in the acceptance of cases after the initial reports are filed, or beforehand, if the case is truly an emergency, the physician then fulfills his strictly professional obligation to the patient in providing all care required by the patient's condition, but with the patient's account carried on a private basis until such time as the problem has been administratively accepted.

From a professional point of view progress notes are a necessity, but such progress notes, in detail, are doubly important in the handling of industrial problems. A statement by the attending surgeon to the effect that the patient is improving means relatively little to either the Claims Department or to the Medical Advisor when the report does not specify as to *how* the patient is improving. Inadequate progress reports do not provide a basis for approval of further physiotherapy or injections which, in the opinion of the attending surgeon, may be indicated. The need for such red tape is developed by a small minority of physicians who, albeit with good intentions abuse the Workmen's Compensation fund with charges for overtreatment.

It is inapropriate to discuss with those of yo here the wisdom of consultation in problem which are, in whole or in part, within the real of other specialties. In such cases there ma again be delay in administrative authorizati for the consultation but with adequate docume tation as to the reasons for requesting such a thorization may be made retroactively and th patient need not lack for care. In many cas expediting of authorization may be affecte

through personal contact or contact by 'phone or letter with the Medical Advisor.

PERMANENT DISABILITIES: Permanent disability rating is the bug-a-boo of the Industrial Commission and of industrial medicine and military medicine and surgery. As you are all aware, however, certain permanent partial and permanent total disabilities are recognized by law and awards on the basis of these disabilities are specifically spelled out. The unilateral losses by amputation are scheduled and the injured workman is compensated at 55% of his established wage rate over a specific number of months. When the attending physician or consultants have determined the extent of permanent partial functional loss of one extremity, again the Commission has a relatively simple job of making an award on the basis of 50% of the established wage rate, again for a specific number of months. Of course, in many cases the extent of permanent partial functional loss is only rather crudely estimated by those of us dealing with these problems.

However, as you know, our greatest problems arise from the unscheduled, or general physical disabilities, which result from combined permanent partial disabilities of two or more extremities, an extremity and an eye, the common spinal injuries, coronary occlusion, and brain trauma, etc. Some of our problems in this regard might be solved if we were able to use the guides to the evaluation of permanent impairment published by the A.M.A. Committee on Medical Rating of Physical Impairment. However, these guides have no practical value under the laws of Arizona, nor after the precedents established over 35 years of functioning under this law. Estimates of general physical disability by attending surgeons and consultants, however, do not much influence the actual financial remuneration for permanent disability awarded the injured workman. The estimate of general physical disability is recorded for comparison with future estimates, and the compensation for general physical disability is determined after the patient's condition has become stationary, or relatively so, and is based on 65% of the difference between his average monthly wages before the accident and the amount which represents his reduced monthly earning capaicty resulting from the disability attributable to the industrial injury. The earning capacity of the workman is determined over a specified period of time proir to the injury and over a similar specified period of time after the condition has become stationary. As you are aware, this provides the injured workman with little motivation to return to gainful employment, or with specific motivation to return to gainful employment at a substantially reduced wage. When an award has been made on the basis of the determined loss of earning power, and the patient is then receiving monthly compensation checks, he may then find himself able to return to his former occupation at a similar wage level with no objective evidence of increase in his physical functional capacity. Previous permanent disabilities are taken into consideration. If a man, as a result of a previous non-industrial injury has an estimated 25% general physical disability following which he sustains an industrial injury which results in an additional 25% physical disabiliity, making a total of 50%, his monthly compensation would, in theory, be only half of what it would be if the entire 50% physical disability were attributable to a single industrial accident.

OCCUPATIONAL DISEASE LAW: Occupational diseases recognized by the statutes of Arizona are specifically listed in most instances and include such problems as anthrax, glanders, tularemia, asbestosis, chrome ulceration or poisoning, dermatitis caused by direct contact with a variety of compounds, impairment or loss of vision due to acetylene or electrical arc welding, pemphigus and erysipeloid due to handling of meat products, poisoning by a number of specifically listed chemicals, metals and their compounds and silicosis. Also, included under the law are blisters or abrasions, synovitis, tenosynovitis, bursitis, cellulitis and ganglions, which may be due to continual pressure or friction or to repeated trauma or vibration of tools. It must be noted that these listed are not due to a specific accident. History-taking by the physician in this type of problem is most important. Under the Workmen's Compensation Law for injury there is, relatively speaking, no statutory limit to the medical benefits and compensation which may be received by the patient. However, under the Occupational Disease Disability Law the dollar value of the benefits received is limited to a maximum of $7500. In the rare instance this may work a hardship on the employee with an in-

dustrial illness. Such limitations were probably written into the law at a time when silicosis was the rule rather than the exception among hard rock miners. A variety of safety factors have reduced substantially the incidence of extensive silicosis among younger miners, but of course, through the years, with increasing industry in Arizona, other industrial hazards have arisen. Presumably we may in the future anticipate difficulties with radioactive substances. I repeat that history-taking by the attending physician is important to assist the Industrial Commission in determining under which law, if either, its responsibiity for the workman's problem, falls.

PLANS FOR THE FUTURE: As most of you are aware, the Gompers Memorial Clinic Rehabilitation Center instituted an Industrial Services Program in early October, 1960. This program has developed after some investigation of similar work-hardening programs in other parts of the country. It has been long recognized by the Industrial Commission and by those dealing with industrial problems that many patients require a program of physical rehabilitation and conditioning after protracted periods of inactivity necessitated by industrial injury and treatment therefor. The Industrial Services Program at Gompers has been set up to provide the place and the personnel to supervise, instruct and encourage such efforts. We are also aware of the innumerable workmen, most specifically in the laboring class, who are deemed able to return to light work by their attending physician, but who, because of the nature of the work to which they are accustomed, are unable to, or fail to return to gainful occupation on a light work status because employers will not provide or do not have light work available. The Industrial Services Program provides the equivalent of light work, under trained supervision, for eight hours a day, five days a week. If physical rehabilitation is not actually accomplished under the program, at least the patient has been observed and the observations recorded to the benefit of the attending surgeon and the Industrial Commissio. We anticipate a gradual expansion of this pr. gram over a period of years.

Having had transmitted to us the tacit a. proval and encouragement of the orthopedis., neurosurgeons and psychiatrists of Tucson, i. vestigation is being made into the feasibility of providing the services of an Industrial Commission Medical Advisor to the doctors in the Tucson area. The purpose of this is not to extend the policing of the professional handling of industrial problems, but rather to provide the services of a Medical Advisor to the doctors of the area to maintain satisfactory relationships with the Industrial Commission, and to increase the effectiveness of consultations which may be held. Consultation reports which are satisfactory from only a medical or surgical viewpoint, frequently do not assist the Industrial Commission in fulfilling its administrative functions in the individual case.

CONCLUSIONS: After having rambled over a variety of subjects with little discussion of purely medical and surgical subjects, I would like to conclude with the comment that— as physicians our responsibility to the injured and sick workman goes beyond the purely medical and surgical. We must, as clearly as possible, establish the relationship of the patient's symptoms and objective findings to a specific accident or occupation, and must clearly report objective findings as well as subjective complaints.

I am amazed at my temerity in discussing the subject at all in the presence of Dr. Moore with his 23 years in the field. I appreciate your courtesy and attention and assure you of our interest in maintaining freedom of medical practice through encouraging adherence to the requirements of the laws, as they now exist, and thereby obviating the need for further control and restriction.

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There is now an average of 2.2 hospital employees for each patient treated in a general hospital, compared with 1.5 in 1946.

(American Hospital Association)

# Insanity

William B. McGrath, M.D.

*An understanding, an explanation, of interest to all practitioners. Review it.*

A SLOGAN of the Mental Health Association is: "The Mentally Ill Can Come Back." The mentally ill can come back from where? From the past. One is mentally ill to whatever extent the unremembered past is distorting his life in the present. Isn't there a saying (Santayana) that those who refuse to study history are doomed to repeat it? If one neglects to understand his personal history, he may go on treating present situations in ways that were appropriate in earlier times and places. Repetition compulsions are among the commonest problems in psychopathology.

The police bring us a transvestist, a man who steals and wears women's clothing. During his childhood he was threatened and dangerously abused by an older brother. Literally to save his life he often had to seek the protection of his mother. Periodically in adult life he has an intense uneasiness in the world of men. He can no longer have the security of being close to his mother's person. So he will take the nearest thing to it, her clothing. And in doing so he feels mixed emotions of shame and relief, like a child who runs to hide in mother's skirts. His transvestism is a compulsion, the undertow of the past.

Now explanations or interpretations like this sometimes sound pretty far-fetched. There are a lot of jokes about them. Pseudo-intellectuals are disposed to go beyond humor to scoffing and sarcasm. Well, ridicule is easy if you have only surface acquaintance with psychiatry and if you do not have responsibility for the care of the patients. Behind the jokes there is a deadly seriousness to our work. Hour by hour, day after day, we see individuals whose lives have become a horrible nightmare. We need the jokes but we ask also for your moral support when our investigations take us into the occult and terrifying depths of insanity.

Insanity is like a nightmare or a dream. The dreamer is the madman sleeping. The madman is the dreamer in action.

When we are dreaming or when we are otherwise irrational, we are not really out of touch with ourselves. On the contrary, it is while dreaming that we do feel the touch of the unknown person within us. The imprisoned mind looks out through the eyes of the past, through the eyes of the animal, the brute, the savage and the child. We had rather not remember our brute origins. But the brute is there in the mind and brain, just as vestiges of the mammalian past are still to be found in the human body.

In the partial disturbances of the mind, the neuroses, we detect influences of the earlier years of the individual. In the total insanities, we seem to be witnessing eruptions from far more remote regions of the mind, possibly from the dim childhood of the race itself.

A fine young man, father of three little boys, went out on the desert, lay down naked and died in the sun. It was some hideous primordial sacrifice. A college professor spent all day stripping the insulation from electric cords, wrapped himself up in them, and then plugged in the circuit.

Presented at the Clinical Club Annual Dinner, May 11, 1961, Phoenix, Arizona.

He had sentenced himself to the electric chair. He left me over seven hundred pages of closely written gibberish with all kinds of cabalistic drawings. Should we laugh at his writings and toss them aside? No; especially when we learn that he had, in fact, killed and mutilated a child. When he killed the child and when he wrote to me, his mind was operating at levels inherited from an aboriginal, subhuman past. His incoherent ideas and strange drawings are unmistakably similar to some of the most primitive findings of the anthropologists.

In the world of insanity, you see, we do listen to an archaic language which we are desperately trying to understand. It is the language of the unconscious, the language of the past.

These subhuman regions of the mind are best exhibited to us in dreams. Internal events or conditions, particularly the blind gropings of the instincts, can hardly be understood or packaged in verbal memory. Hence there is little representation of ideas by words and none by ordinary grammar or logic. Most of the imagery is visual. And it is symbolic and enormously condensed. This seems hard to comprehend until you recall that the slightest gesture, even in waking communication, can convey more than a thousand words. The lift of an eyebrow or a pursing of the mouth can indicate a world of disbelief or expectancy. A patient swallows or licks his lips or looks flustered when a word or remark, even by remote association, prods some timeless urge below the surface of consciousness.

So we observe not just the incoherent language but the primitive and magical gestures of the insane. You are familiar with some of the symbols and rituals of the neurotic: the handwashing of guilt, the compulsive orderliness of the individual whose inner house is in anxious disorder, the hundreds of irrational acts which simultaneously hide and yet betray what is going on in the deeper regions of our minds.

At these levels, associations are quite loose. Matters or figures that are in any respect similar promptly become identical. Again, in everyday life we see the immature individual substituting any and every authority figure for the first authority to whom he reacted. In a dream or delirium a whole notion may be represented by its opposite or by some small part. This, to occurs in sarcasm and poetry and in ordinar conversation. One says, "Boy, is he modest meaning the opposite. Or one jumps from a pa ticular observation to express a universal opinio

In the unconscious, in the mind of the preve bal child and the brute, there are no dimensio of time and space. Everything is fermenting the same cauldron. There are no concepts closer or further, earlier or later. And the d mand for gratification of an urge is like a refle immediate and heedless, like a reptile or a fis striking its prey. Does this seem absured? The examine the man who, after drinking some win raped and murdered the only available victim, a helpless child. Or talk to the quiet lad who suddenly goes berserk and kills everyone in sight.

In every one of these tragic disorders nature has given us warnings. But people have paid no attention to them. It is disturbing to note the reluctance, even resistance, of most people to study the workings of their own minds. We had rather discuss the superficial relationships of the individual to others and to his present environment. We prefer to believe that pretty sentiments and good will hold the answers to mental disease.

We ask a nervous person, "Have you been having dreams?" And he shrugs it off: "I suppose so, but I don't pay any attention to them."

Why not? He would surely be alerted if there was a swelling or a rash on his body. Every physical symptom is a clue to disease or disorder in the organism. If a piece of shrapnel or a splinter should be lost in your tissues, the body will work unceasingly to be rid of it. And finally it will erupt, perhaps after many years and in a distant place. The mind, too, will never re until it can have disgorged into consciousnes any impediment to our well-being and progres

These impediments, the unfinished business the past, betray themselves in mental symptom You cannot afford to disregard a mood of i explicable disquiet and restlessness. You ha better pay close attention to your lapses memory, your slips of the tongue, your ove valued ideas, your occasionally inappropria

emotional reactions, your private superstitions and rituals. All of these symptoms — and especially your dreams — are clues to trouble in the mind.

People who are afraid to think about themselves are afraid of everything. This is not necessary and it is not safe. You do not need to build ever more frantic defenses of denial and repression to wall off the unconscious. The unconscious can be understood if you learn its language. The better you come to know the unconscious, this living representation of your own past and our whole racial origins, the freer you are. For then all of its energies become available to the waking and reasonable mind, instead of boiling and fermenting in vague nervous tension or erupting in the primitive and nightmarish excitements which we treat.

How do we learn the language of the unconscious? As in any science we gather data. We record our observations and see what information others have accumulated. We observe the effects of hereditary and acquired diseases of the brain and the influences of drugs on behavior. We study animals in laboratories where each of the environmental variables can be controlled and evaluated. We know something of what happens to children in orphanages and prisoners in concentration camps. We listen to the drums and rhythmic incantations of propaganda. We see the breakdown from civilized to barbarian to savage to predatory behavior when the individual has relinquished his soul to the mob. Most of all we try not to disregard any detail of the actions and reactions of our patients.

When they express themselves in symbolic gestures or incoherent words, we turn to all the other disciplines in which the human mind has tried to explain and come to terms with itself.

We cannot then ignore the most modern or the most primitive art; the most harmonious or discordant music, the most aboriginal or the most current history and philosophy and science.

Somewhere in the incredibly profuse and complicated data there is a theme or a message which nature is trying to convey to us. We never forget that nature is infinitely wise. A million or a billion years ago the tiny living cell was storing and transmitting more information than today's most elaborate computing machine. Equations which made atomic energy possible were already valid at the time of creation. The scientific discoveries of the future, especially in psychiatry, will simply be recognition of what nature has been trying to tell us all the time.

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## Third Annual Award for Prize-Winning Paper
## 1962 Annual Meeting

March 15 is the deadline for accepting original papers to be entered in open competition and judged by the Scientific Assembly Committee for the third annual award.

The Association has established this award "to stimulate research and original clinical effort" and to recognize the best scientific presentation by an Arizona physician.

The successful entry will be read by the author during the convention, and the award, a bronze plaque, will be presented at the president's dinner dance.

## Section on Roentgenology

# Acute Cholecystitis Emphysematosa

## A CASE REPORT

**Frank M. Behlke, M.D.**

CHOLECYSTITIS, emphysematosa, an uncommon disease, occurs when certain gas producing bacteria invade the gallbladder, causing inflammation. The accumulation of gas within the gallbladder, and at times, the pericholecystic tissues, presents a characteristic appearance on plain roentgenograms, obviating the use of contrast materials in arriving at the correct diagnosis.

In 1901, Stolz(1) described three cases of gas within the gallbladder at autopsy. He contended that the biliary system was invaded terminally by gas bacilli the gas actually accumulating after death. Welch and Nutall(2) thought it likely that bacterial invasion could occur during life, but the gas production was a post-mortem phenomenon. It was obvious that both invasion and gas production occurred during life when Lobingier(3) in 1908, at operation, discovered an emphysematous gallbladder. Hegner(4) was the first to report the preoperative diagnosis of "gaseous pericholecystitis," from a flat film of the abdomen in 1931. The causative organism cultured was Clostridium welchii. Since then the majority of reported cases have been due to Clostridium welchii or Escherichia coli, alone or in combination. Other organisms cultured have been Aerobacter aerogenes, Staphylococcus albus, streptococci and an atypical gas producing Actinomyces(5). The purpose of this communication is to report a case of emphysematous cholecystitis and present a brief review of the medical aspects of this interesting problem.

### CASE REPORT

A 60-year-old white male was first admitted to the Tucson Medical Center on September 24, 1960, with acute right upper quadrant pain associated with nausea and vomiting of 24 hours' duration. The patient had similar symptoms in the past, but less severe, and at another hospital a diagnosis of gallbladder disease was made. There was no previous history of jaundice, dark urine, or clay colored stools.

Physical examination revealed a well nourished male in acute distress. The skin was pale and moist, without icterus. Spider nevi were not present. The sclerae were of normal color. There was marked right upper quadrant tenderness and rigidity with absent bowel sounds. The highest temperature was 100.2°F on the second hospital day. Pulse was 50 per minute on admission with a blood pressure of 140/100. WBC 18,000 per cubic mm.; hemoglobin 14.0 gm. per cent; hematocrit 42.5 vol. per cent; VDRL non-reactive; urinalysis showed a few RBC's and WBC's per high power field with a specific gravity of 1.028. Liver function studies were excluded.

The diagnosis was an acute exacerbation of chronic cholecystitis and the patient was placed on bed rest with nothing by mouth, given pain relieving drugs and I.V. fluids to restore hydration and electrolyte balance. An EKG was abnormal showing left ventricular hypertrophy with no evidence of recent myocardial infarction. On the first hospital day an intravenous cholangiogram demonstrated normal calibre hepatic and common bile ducts and no evidence of calculi. The gallbladder did not opacify. Contrast material was identified in the duodenum. On the second hospital day, an oral cholecystography study failed to demonstrate gallbladder visualization, however, the gallbladder was filled with gas. Air was not seen in the ductal system. Lateral decubitus films demonstrated a gas-fluid level present within the gallbladder. A diagnosis of acute cholecystitis emphysematosa was made. Subsequent to this, an upper gastrointestinal series was performed demonstrating irritability of the duodenal bulb and duodenal loop, apparently on the basis of the acutely inflamed gas filled gallbladder (Fig. 1a). No free communication between the biliary tract and the duodenum could be demonstrated. The right upper quadrant pain disappeared and he was discharged on the third hospital day to return in one month for cholecystectomy. He was readmitted, however, 24 hours after discharge with a severe exacerbation of symptoms. A roentgenogram of the right upper quadrant continued to show gas within the gallbladder with air also in the intramural portion but not in pericholecystic tissue (Fig. 1b). Again, with conservative management consisting of bed rest, intravenous fluid, analgesics and an antibiotic his symptoms subsided and he was discharged on the third hospital day of the second admission.

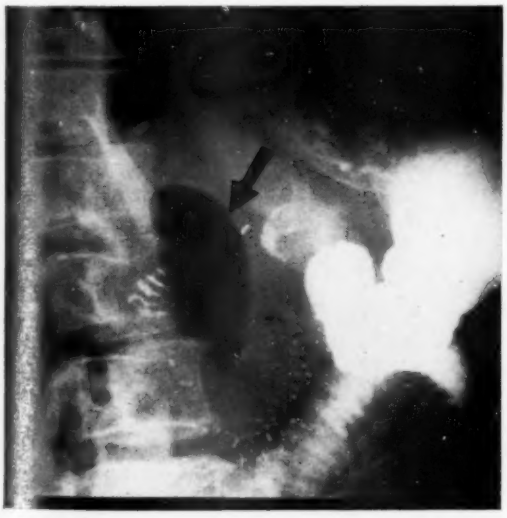

**Fig. 1a.**

**Right anterior oblique projection obtained during an upper gastrointestinal series demonstrating gas within the gallbladder without demonstration of a free communication of the biliary tract with the intestine.**

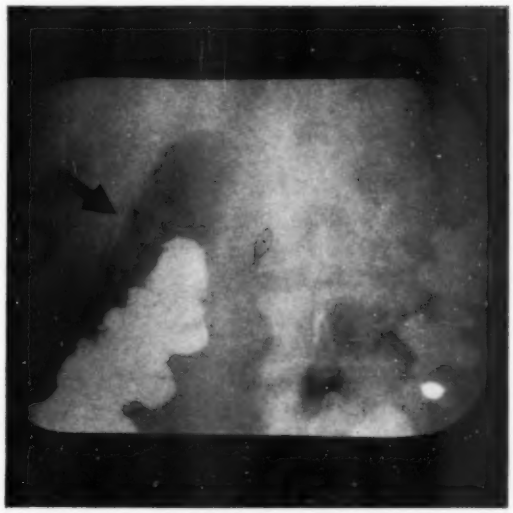

**Fig. 1b.**

**Anteroposterior film study obtained on the second hospital admission showing gas has dissected into the wall of the gallbladder which remains well outlined. Barium is present in the colon, the residual from a previous upper gastrointestinal series. Air is not present within the biliary tract but several cases of emphysematous cholecystitis have been reported demonstrating ductal gas.**

On the third and final admission, approximately one month following establishment of the diagnosis, a cholecystectomy was performed and a markedly contracted, thick and edematous, and subacutely inflamed gallbladder was removed. The cystic duct contained small stones. A culture was not obtained. Pathologic report was chronic cholecystitis and pericholecystitis with gangrene and cholelithiasis. The patient made an uneventful postoperative recovery.

## DISCUSSION

A review of the literature reveals that, clinically, the patient with this malady presents with typical gallbladder symptoms and signs. Nausea and vomiting associated with upper abdominal pain localizing to the right upper quadrant is invariably present. In over half of reported cases

a palpable mass in the gallbladder region has been found. Jaundice may be noted and the temperature elevated between 99° and 103°F in conjunction with a high white blood cell count. Diabetes mellitus has been reported in approximately one-half of reported cases and calculi have been found about 50 per cent of the time. Just the converse of usual cholecystitis, men outnumber women 3 to 1(6) with the highest occurrence in the 5th and 6th decades. More than 80 per cent of patients have been over 50 years of age, with the over-all range of 27 to 75 years.

## RADIOLOGIC ASPECTS

Basically, the diagnosis can be established on plain film examination of the right upper quadrant with the patient prone, erect or in the right lateral decubitus position. A fluid level will frequently be encountered in the upright and decubitus projections. The time interval for the gas to appear after onset of symptoms is variable but usually within 72 hours sufficient gas will have accumulated to be of diagnostic import.

As the gallbladder distends there is dissection of gas between the muscularis and mucous membrane as described by Freidman, Aurelius and Rigler(7). The infection may become severe enough that abscesses containing gas and fluid appear in the surrounding cholecystic tissues. Rarely the inflamed gallbladder may perforate and gas appear beneath the diaphragm as reported in two patients by the Rabinovitchs, Pines and Lipton in 1958(8).

Basically, as presented by Jacobs(9), there are four methods of gas entering the gallbladder: (1) Infection of gallbladder by gas forming organisms; (2) Surgical procedures such as cholecystojejunostomy or choledochojejunostomy; (3) reflux of air from the duodenum through a relaxed sphincter of Oddi and (4) spontaneous cholecysto-enterostomy. In the differential diagnosis, lipomatosis of the gallbladder may be considered but in this instance there is no gas within the gallbladder, there being just a slim lucent rim outlining the wall.

In this case, Skokan's(6) criteria for establishing the diagnosis was met; namely, (1) presence of gas in the lumen of the gallbladder and gas infiltration of the wall; (2) typical clinical symptoms of acute cholecystitis; and (3) e- clusion of pathological communication of t gallbladder and biliary tree with the digesti tract.

## TREATMENT

Grainger(5) has advocated operating prior the appearance of intramural gas and waiting f this appears before a cholecystectomy can e performed. Jacobs(9) reports two cases operate upon four days and eleven days after roentge diagnosis of gas within the gallbladder, both f these making a satisfactory recovery. Preoperative polyvalent gas gangrene antitoxin, antibiotics and restoration of fluid and electrolyte balance are recommened along with bed rest and analgesics. The danger of rupture of the gallbladder with peritonitis or abscess formation is a possible complication to be treated with antitoxin and antibiotics as the situation warrants. Cholecystectomy is the procedure of choice although cholecystostomy may be indicated if rupture or abscess formation are found on exploration. Complications such as pulmonary embolism and severe sepsis have been reported. In this presented case, conservative treatment followed by cholecystectomy in one month after subsidence of symptoms provided an excellent recovery without complications.

## SUMMARY

A case of cholecystitis emphysematosa is reported with a review of signs and symptoms, etiology, roentgenographic diagnosis, and treatment.

The plain abdominal film study of the right upper quadrant demonstrating a gas distended gallbladder frequently with gas-fluid level in the decubitus projection is diagnostic of this disease.

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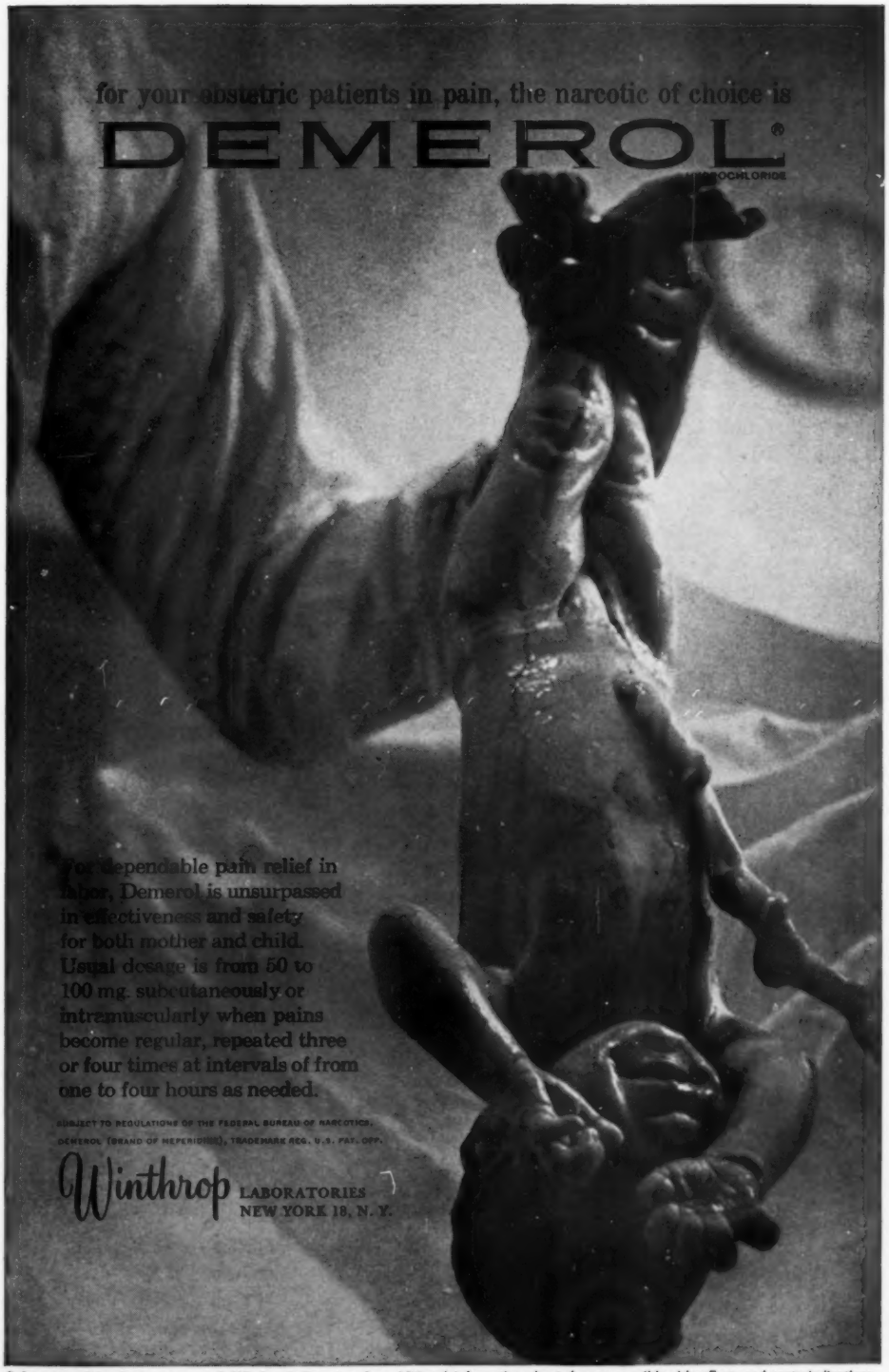
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*Gamble, C.J.: Am. Pract. & Digest. Treat. *11*:852 (Oct.) 1960. See also Berberian, D.A., and Slighter, R.G.: J.A.M.A. *168*:2257 (Dec. 27) 1958; Kaufman, S.A.: Obst. and Gynec. *15*:401 (March) 1960; Warner, M.P.: J.Am.M. Women's A. *14*:412 (May) 1959.

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## The President's Page

# Greetings

Leslie B. Smith, M.D.

The Yuletide with its admixture of the tenets of religion and make-believe provides an opportunity to manifest our devotion and relax our tensions by reversion to the fantasies of childhood.

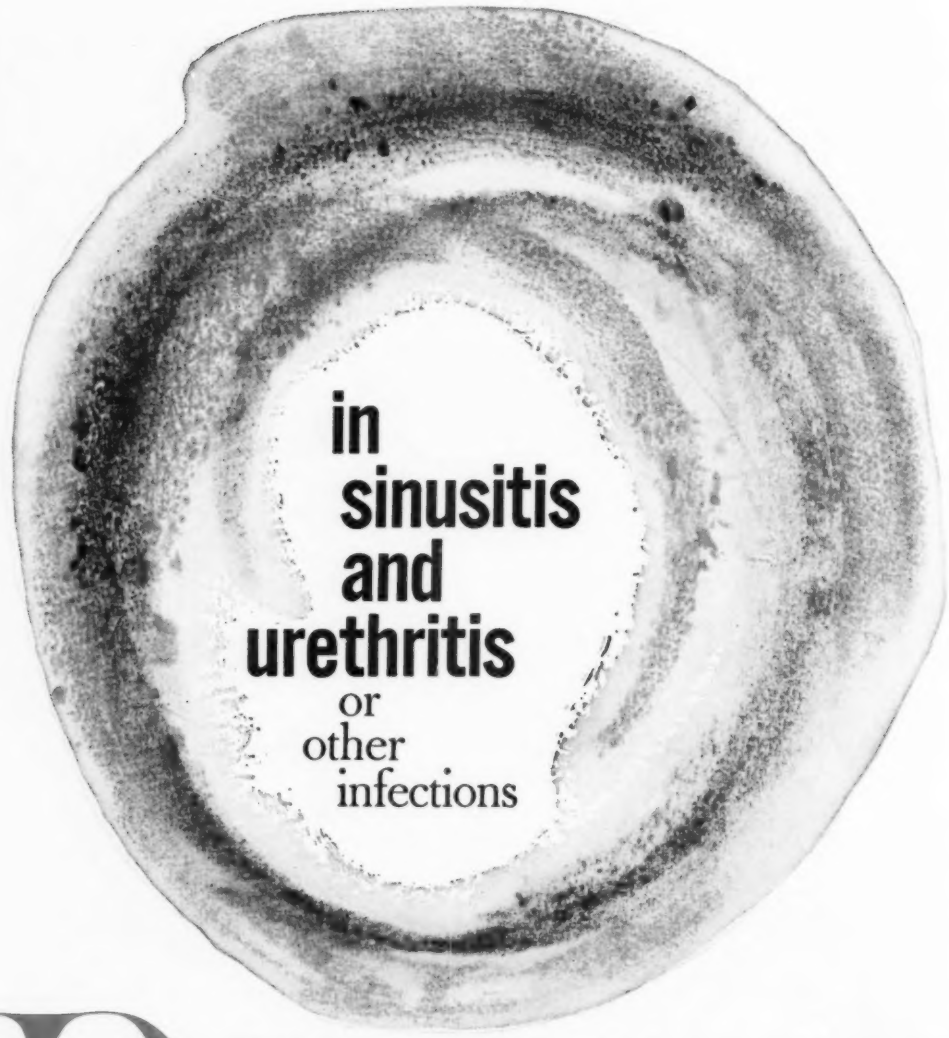
The accumulated frustrations, resulting from our everyday endeavors to achieve our goals and to adapt to the many facets of our changing environment, make this season a most necessary respite.

We should enhance our stature by mixing the Birthday festivities with more serious deliberations – by seeking good where there is known evil – tempering our aversions with tolerance – modifying our hates with humanism – reducing our selfishness with altruism and we, as physicians, must strive to compensate for our indifferences with more loving, tender care.

Although there is balm in the temporary participation in the fantasies of Santa Claus, we must maintain realism in our acceptance of doctrines – by acknowledging that "there is no Santa Claus."

May the merriment and the morality of this Yuletide augment your happiness during 1962 and all the years to follow.

Leslie B. Smith, M.D.

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## Editorials

# Have M. D., Will Travel

Have you ever had the urge to go somewhere or do something different, making use of your medical training? Most doctors dream of a "sometime" when they can sign on as a ship's doctor and sail to remote and romantic parts of the world or perhaps go along as medical advisor for some scientific exploratory expedition or find some other adventure – some fruition for their day-dreams and utilization of their medical training.

A group of five physicians in Tulsa, Oklahoma have found a way to do something about these desires and at the same time to render a soul satisfying sort of medical service. These five men who are members of the Presbyterian Church of Tulsa, Oklahoma, are giving up their practices for six week periods to serve voluntarily at the Miraj Medical Center in Miraz, India.

And now it may be news to you to know that the A.M.A. has a new department of International Health which administers a program approved by the House of Delegates last June whereby any member of the A.M.A. may volunteer for service in the foreign mission fields on a temporary basis when emergencies arise. Missionary agencies representing every major de-


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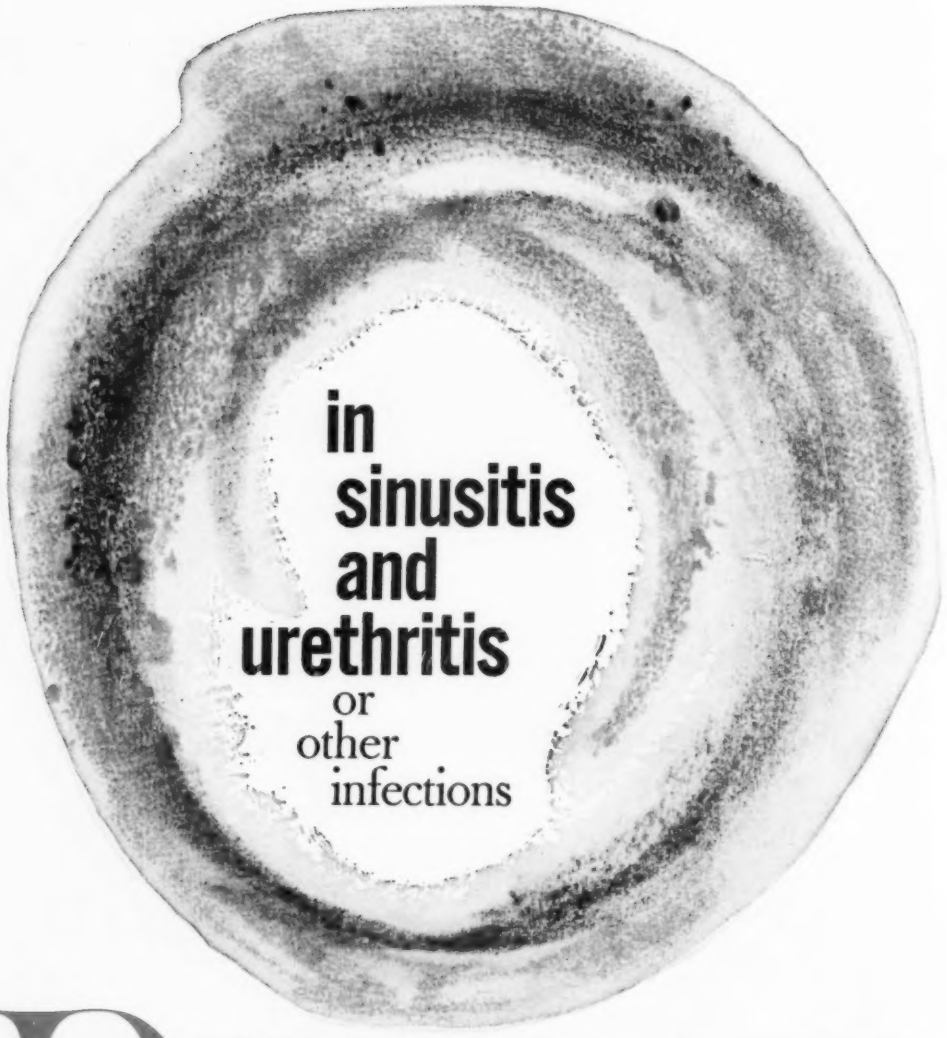


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R. Lee Foster, M.D.

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## EDITOR'S NOTES

(Following notes are taken from "The Effects of Nuclear Weapons on Tucson," by Thomas L. Martin, Jr., Dean, College of Engineering, The University of Arizona, published October, 1961 by The University of Arizona Press, Tucson.)

" . . . following conditions will have to be met for Tucson shelters:

(1) They must be at least 4 feet underground and preferably 5 feet . . .

(2) They must take at least 5 psi of peak overpressure, and preferably 20 psi . . .

(3) The shelters will most likely be occupied full time for at least one month . . . and part-time for much longer periods."

"But we must recognize also that weapons of war are evaluated according to their usefulness in the achievement of military, economic, and political objectives. The relative horror of a weapon does not figure in this evaluation except in its potential for intimidation."

" . . . much of the military effectiveness of nuclear weapons depends upon lack of preparation for civilian defense. If the population is sheltered and prepared, nuclear weapons are far less attractive and less useful."

"It is vital that the people of Tucson understand that they *can* survive a nuclear attack on Tucson if, and *only* if, they are in a well-designed shelter."

" . . . if you have a shelter, the chances are at least 7 out of 10, and probably better, that you will survive the attack. The odds may be slightly different in other parts of the country, but not significantly. Thus, there is no reason to run away from Tucson."

* * *

" . . . KILOTONS (thousands of tons of TNT) and MEGATONS (millions of tons of TNT."

" . . . *air bursts* are used against targets which are most easily damaged by overpressure."

" . . . air bursts are ineffective against har ened targets . . . "

" . . . *surface bursts* are used to destroy ha *targets* . . . "

"Davis-Monthan is a "soft" target."

" . . . so it is reasonably realistic to assu that an attack on Davis-Monthan will use eit a 2 or a 5 megaton air burst."

"Very little fallout is produced by an *air bu* even in the immediate vicinity of ground ze Thus, in the event of an air burst over Dav Monthan, in the megaton range, there would very little fallout and it would be necessary occupy underground shelters for only a fe days at the most."

" . . . shelter planning in Tucson should as sume that shelters will be occupied for as muc as four to six weeks in the event of an attack on Davis-Monthan."

"It is believed that the rocket booster used to orbit the spaceships Vostok I and II could easily deliver a warhead with a yield of 25 megatons or more, anywhere in the United States."

" . . . the radiation received by sheltered personnel because of the initial radiation must be held below 50 roentgens. Indeed 50 roentgens must be taken as the absolute maximum permissible; ideally it should be 5 or less."

" . . . *accumulated* dose, though spread over several weeks, will produce essentially the same effects at about the same levels of radiation as the single exposure effects . . . "

* * *

WHOLE BODY, SINGLE RADIATION DOSE EFFECTS(1)

| Single Radiation Dose in 24 Hours | Clinical Effects |
|---|---|
| 0 to 25 roentgens | none |
| 25 to 50 roentgens | some genetic effects; no serious clinical effects |
| 100 roentgens | nausea and fatigue |
| 125 to 150 roentgens | vomiting becomes a problem |
| 200 roentgens | some fatalities 2-6 weeks later; nausea, vomiting, and fatigue within 24 hours; sterility, temporary or permanent |
| 400 roentgens | immediate incapacitation from which many never recover; some deaths in 2-6 weeks. |
| 600 roentgens | assumed fatal in 100 per cent of the cases |

" . . . children under 18 should not receive a radiation if it can be avoided. Doses of 5 roe

(1) Excellent radiation measuring equipment may be obtain for $19.95 plus tax by writing to The Bendix Corporation, 31 Wasson Road, Cincinnati 8, Ohio. This includes a dosimet rate meter, and calibrating device, and is called the "Fam Radiation Measurement Kit."

gens or more will show up as genetic defects in their decendents."

". . . 3 feet of earth cover provides an attenuation factor of 25."

". . . 4 feet of earth cover seems to be the minimum desirable for Tucsonans, and 5 feet would be ideal."

**ATTENUATION OF INITIAL RADIATION BY EARTH**

| Depth of Earth Cover in Feet | Attenuation Factor |
|---|---|
| 2 | less than 10 |
| 3 | 25 |
| 4 | 70 |
| 5 | 220 |
| 6 | 1000 |

**ATTENUATION FACTORS AGAINST FALLOUT RADIATION**

| Depth of Earth Cover in Feet | Attenuation Factor |
|---|---|
| 2 | about 70 |
| 3 | above 1000 |
| 4 | above 100,000 |
| 5 | nearly infinite |
| 6 | nearly infinite |

**FALLOUT RADIATION REDUCTION FACTORS**

| Time in Hours After the Explosion | Radiation Reduction Factor |
|---|---|
| 1 | 1.0 |
| 5 | 0.150 |
| 10 | 0.063 |
| 24 (1day ) | 0.022 |
| 168 (1 week) | 0.00215 |
| 336 (2 weeks) | 0.00093 |
| 672 (4 weeks) | 0.00040 |
| 1008 (6 weeks) | 0.00025 |

"There will be 300 or more Titan and Atlas missiles in place when the nationwide system is complete in about 1964 . . . "

". . . President Kennedy . . . September 25, 1961 . . . "

"Every man, woman, and child lives under a nuclear sword of Damocles, hanging by the slenderest of threads, capable of being cut at any moment by accident, miscalculation, or madness."

"We must be prepared for any eventuality; for Tucson this means preparation for the possibility of two 10 megaton, or one 20 megaton, attack against each of the Titan silos surrounding Tucson."

". . . if a shelter is designed to survive an air burst over Davis-Monthan Air Force Base, it will, in all probability, survive the blast effects of an attack against the Titan bases."

". . . the primary concern of Tusconans, relative to an attack on the surrounding Titan bases, is *fallout* because the other effects prove to be relatively unimportant."

• •

". . . serious fallout over Tucson no matter what the wind direction may be."

"As a result, from the radiation levels . . . it seems very likely that the 1-hour reference radiation from fallout

(1) *cannot possibly be less than 15,000 to 20,000 roentgens/hour.*

(2) *could very probably be much more than 20,000 roentgens/hour, conceivably as high as 100,000 roentgens/hour if there is a great deal of overlapping of fallout patterns."*

• •

". . . 3 feet of earth provides a fallout attenuation factor of about 1000."

". . . using *at least* 4 feet of . . . "

"The extra foot of earth cover is the cheapest insurance available. Five feet of earth cover would reduce this radiation dose to a negligible figure."

• •

". . . in the event of an attack on the Titan bases, Tucsonans will be in their shelters almost continuously for 4 weeks and intermittently for many additional weeks. At the very least, shelter planning must assume 4 weeks of occupancy. Conservative planners will consider very strongly the possibility of occupancy for 6 weeks continuously."

• •

"(1) Shelters should be at least 4 feet underground, and 5 feet would be preferred. No advantage is secured by going deeper.

(2) Shelters should be designed to resist blast overpressures ranging between 5 and 25 pounds per square inch, depending upon the shelter location relative to Davis-Monthan.

(3) Air-vent pipes and other structures above ground will be subjected to horizontal pressures which
   (a) will probably be only about 3½ pounds per square inch, but
   (b) could rise as high as 15 to 40 pounds per square inch, though this is unlikely.

(4) Shelter doors and entrances must be able to withstand overpressures in the range of 5 to 25 pounds per square inch without buckling or jamming.

(5) A second, emergency escape hatch must be provided in the event that the main entrance is damaged or heavily covered

by rubble. This can usually be made available by a removable plate inside the shelter and sand packed above it when the shelter is backfilled. This makes it easy to dig out.

(6) The shelter should be large enough and well enough stocked to permit occupancy for one month or longer. A wise precaution would be to provide nearby, buried caches of extra supplies which could be gotten within a short period of exposure outside the shelter.

(7) The air filter should be shielded by steel so that it will not be ignited by the thermal blast.

(8) The shelter entrance should have at least two right turns in it and should be at least 2 feet away (and preferably 3 feet from the main structure of the shelter.

"*All of these structures should have curved or domed roofs,* the greater the curvature the greater the strength. There are some prestressed, precast reinforced concrete shelters being designed for use in Tucson according to the blast resistant requirements specified herein."

NOTE: Dr. Thomas L. Martin, Jr.'s booklet, "The Effects of Nuclear Weapons on Tucson," can be obtained from the University of Arizona Press, Tucson, at $1.00 per copy.

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## CHEMOTHERAPY OF BREAST CANCER

To attempt to cover this material is to cover a segment of medical therapy that is extremely controversial. One can probably differ with almost every statement made in this summary. However, in my hands the best results have been obtained by following the course of treatment as here outlined and in consideration of this philosophy of treatment.

Chemotherapy of breast cancer falls under two categories:

1. The chemotherapeutic agents, as Thio-TEPA and Cytoxan, etc.
2. The endocrines, as androgens, estrogens, and the corticosteroids.

In the use of the endocrines, 60% of the cases will be completely hormonal independent and will not respond to the endocrine therapy in any way. The anti-tumor effect of the endocrines i breast cancer is not a neutralization of the op posite sex hormone, for there is a normal coe istence of androgens and estrogen. In fact, trea ment with Testosterone not infrequently will i crease the level of estrogens in a patient; an this occurs irrespective of the therapeutic effe attained. The mode of action is apparently a elimination of stimulatory factors by the anteri lobe of the pituitary. An analogy can be draw in considering the action noted wtih the admi istration of thyroid in patients with cancer o the thyroid. Here our experience has been grea er. In these patients by oversupplying the need of the patient with exogenous thyroid, as giving three or four grains per day, there is no stimulus to the pituitary to produce the thyroid stimulating hormone. This latter is essential to the development of the thyroid cancer while the tumor is still in the dependent phase. It is no longer essential when the cancer becomes autonomous. A comparable situation probably exists in breast cancer.

The mammotropic hormone developed by the eosinophilic cell of the pituitary is apparently an important factor in the development or suppression of breast cancer. It is the follicle stimulating hormone that plays a decisive role in all mammary hyperplasia. Its production is suppressed by estrogens in the absence of functioning ovaries. Its elimination probably suppresses breast cancer that is still in the dependent phase. It does not influence the autonomous cancer.

It is striking that prolactin, the lactation stimulating hormone of the anterior pituitary seems to play no role. The mitotic coefficient of the breast is sharply decreased during the period of lactation. Hyperplasia of the mammary glands occurs during pregnancy when the level of the estrogen is increased. Note, this is hyperplasia in the presence of estrogen in a patient with functioning ovaries. With intact and functioning ovaries, estrogens through the pituitary stimulate the production of progesterone. This progesterone stimulates the production of the follicle stimulating hormone of the pituitary. Estrogen alone, however, will inhibit the production of the follicle stimulating hormone. Consequently, only in the post-menopausal female, or in the patient whose ovaries have been removed can estrogens be effective in the repression of breast cancer.

Therefore, in the pre-menopausal female with progesterone present estrogens are contraindicated, but estrogens may prove suppressive in the post-menopausal female or in the patient who has been castrated.

In the pre-menopausal patient who develops metastasis, castration is recommended. This in itself produces the greatest percentage of remissions and over the longest period. Later with an advance in the disease, that is, after castration or in the post-menopausal female, the initial drug of choice seems to be Testosterone Propionate. However, the rational of therapy with this drug makes one question it. It would seem that the mechanism of its action is to raise the estrogen level, essentially by stimulation of the estrogen production of the adrenal cortex; and the estrogen in turn inhibits the production of follicle stimulating hormone by the pituitary. The therapeutic effect of the androgens is always connected with an abrupt fall or disappearance of the follicle stimulating hormone of the pituitary. If a remission is obtained with Testosterone Propionate, and it can be expected in about 35% of the cases, and later control of the cancer is lost, that drug should be discontinued. One should then wait for a short period before starting another hormone. The patient may have a remission as a result of the withdrawal of this hormone. Following this, however, estrogen therapy may prove of help, and possibly helpful in as high as 45% of the cases. In general, the estrogen should be supplemented by cortico-steroids to bring about a medical adrenalectomy.

Castration as the first step in therapy has been recommended, not only for the pre-menopausal female with disseminated breast cancer, but it has been advocated by many for all pre-menopausal patients with breast cancer whether there is clinical dissemination of the disease or not. This is a step I have not been able to recommend. Castration cures no patient; it suppresses persisting disease. The radical mastectomy in itself can be anticipated to cure 80 to 90% of patients with no axillary metastasis. Therefore, this is too great a price to pay, that is, the artificial menopause for the already cured patient, to only bring about suppressive therapy in the patient who has disseminated disease of unknown magnitude.

In the cancer patient with disseminated disease, after control of the cancer is lost with the above measures, that is following oophorectomy, androgens, estrogens and cortico-steroids, adrenalectomy has been recommended. Again, this is a radical step for what little it has to offer. It is known that there is aberrant adrenal tissue, disseminated in the retroperitoneal areas, and this is tissue that cannot readily be located. Similarly, the procedure of hypophysectomy must be questioned. Pharyngeal pituitary cells in a functional state have been found in patients subjected to hypophysectomy, obviously this again limits the potentialities and possibilities of the effectiveness of this procedure. Either of these procedures, hypophysectomy or adrenalectomy, presents a 9% operative and post-operative mortality. A regression of the tumor is noted in 30 to 32% of the cases when one of these steps is taken. The average time from the surgical ablation of that endocrine to death, that is, following adrenalectomy, is 6½ months; it is comparable following hypophysectomy. The results are very similar whether the metastasis have been to bone, soft tissue or viscera. This level of results, with a mortality of roughly 10%, seems to be too ineffective to recommend in view of surgery of this magnitude. One of the strongest proponents of surgical ablative procedures, particularly adrenalectomy, has been Dr. Ian G. Macdonald of Los Angeles; and at the National Cancer Institute meeting he admitted that probably the replacement by the cortico-steroid does all of the work that these operative procedures can do. Consequently, it would seem that medical adrenalectomy by large doses of cortisone or its more refined derivatives is the desirable procedure rather than recommending additional surgery of this magnitude with questionable and limited results.

No chemical thus far studied has demonstrated a high degree of activity against breast tumors. Regression rates are reported between 0 and 30%. Their margin of safety is very narrow. The difference between the therapeutic level and toxic level is that between 1 to 1½ or 1 to 3. The latter figure is for Cytoxan and it has been one of the more ineffective in breast cancer. It is a narrow margin of safety and we nearly always have to see the toxic level of the drug attained before therapeutic effectiveness can be acquired. ThioTEPA has probably had the greatest clinical application and has certainly been the most widely advertised in this area. It should be reserved for those patients who do not respond to

the hormones. However, at the time of surgery it is probably indicated, although its use and effectiveness is not completely proven. It would seem that present statistics show better results by the administration of ThioTEPA at the time of radical mastectomy — probably in doses of 15 mg. intravenously, and the same dosage to be given on the first two days postoperatively. The initial reports would indicate that the recurrence rate is cut down 50% by these procedures. That is cutting down the recurrence rate of the patient without axillary metastasis from a level of 10-20% to 5-10% and for the patient with axillary metastasis from 60-70% to 30-35%.

Dr. Bateman has been a strong proponent of the use of ThioTEPA and does bring an interesting aspect and an alteration in philosophy in the management of this disease. She encourages that we manage this disease as if it were a chronic illness that we will not eradicate, but that we will suppress over a period of time. She uses ThioTEPA both directly into the tumor site and intravenously, at weekly intervals, over prolonged periods varying her dosage somewhat, but making up her solution at 10 mgs. per cc. Effective suppressive results have been noted in some cases by this procedure.

Direct anti-tumor effect with the chemotherapeutic agents is either cytoxic due to direct action upon already present nucleic acids or antimetabolic due to inhibition of nucleic acid formation.

Cytoxic therapy is considered particularly for breast carcinoma if there is:

1. Malignant effusion.
2. An inflammatory type lesion.
3. Metastasis to soft bone and tumors of relatively small bulk.
4. Advanced cases that are not responsive to hormonal therapy.

Chemotherapy is less effective when the predominant metastasis is to bone.

If surgery of any type is contemplated, chemotherapy should not be so intensive as to produce a thrombocytopenia. Further, if there has been recent irradiation therapy or simultaneous irradiation therapy, there is a decreased dose tolerance because of the hematopoietic depression.

Nitrogen mustard was the first of the drugs used at 0.4 mgs. per kilogram intravenously. Tumor control was only attained in 6% of the cases. If it is used as an intracavitary drug, it is used in the same dosage mixing it with 100 cc. of normal saline solution after draining off the cavity. The position of the patient is changed frequently during the first hour after injection. However, during the first 48 hours after the injection, there may be rapid reaccumulation of fluid which necessitates immediate withdrawal of that fluid. It should be used only in those patients with significant symptoms from their effusion.

ThioTEPA shows objective improvement in one-third of the cases. The results at the M. D. Anderson Hospital have not equaled those that have been reported by Dr. Bateman. The initial loading dose is 2.0 to 2.5 mgs. per kilogram during a two to three week period. This is given as 15 mgs. every second day until the white blood cell count drops to 3,000 or less and then continued at a lesser dosage until the total loading dose is obtained. The maintenance dose is 10 to 15 mgs. once to twice per week.

5-Fluorouracil, an antimetabolite, has shown objective regression in 30% of the cases. However, to produce a tumor effect almost invariably there must be toxicity as stomatitis, diarrhea, and/or leukopenia.

Other drugs used with some success have been Amethopterin (28% regression), Nitromin (27% regression) and Cytoxan (25% regression).

---

Some 132 million Americans — 73 per cent of the civilian population — had health insurance at the end of 1960, the Health Insurance Council said in reporting the results of its 15th annual survey on the extent of voluntary health insurance coverage in the United States. The survey is based on reports from insurance companies, Blue Cross-Blue Shield, and other health care plans.

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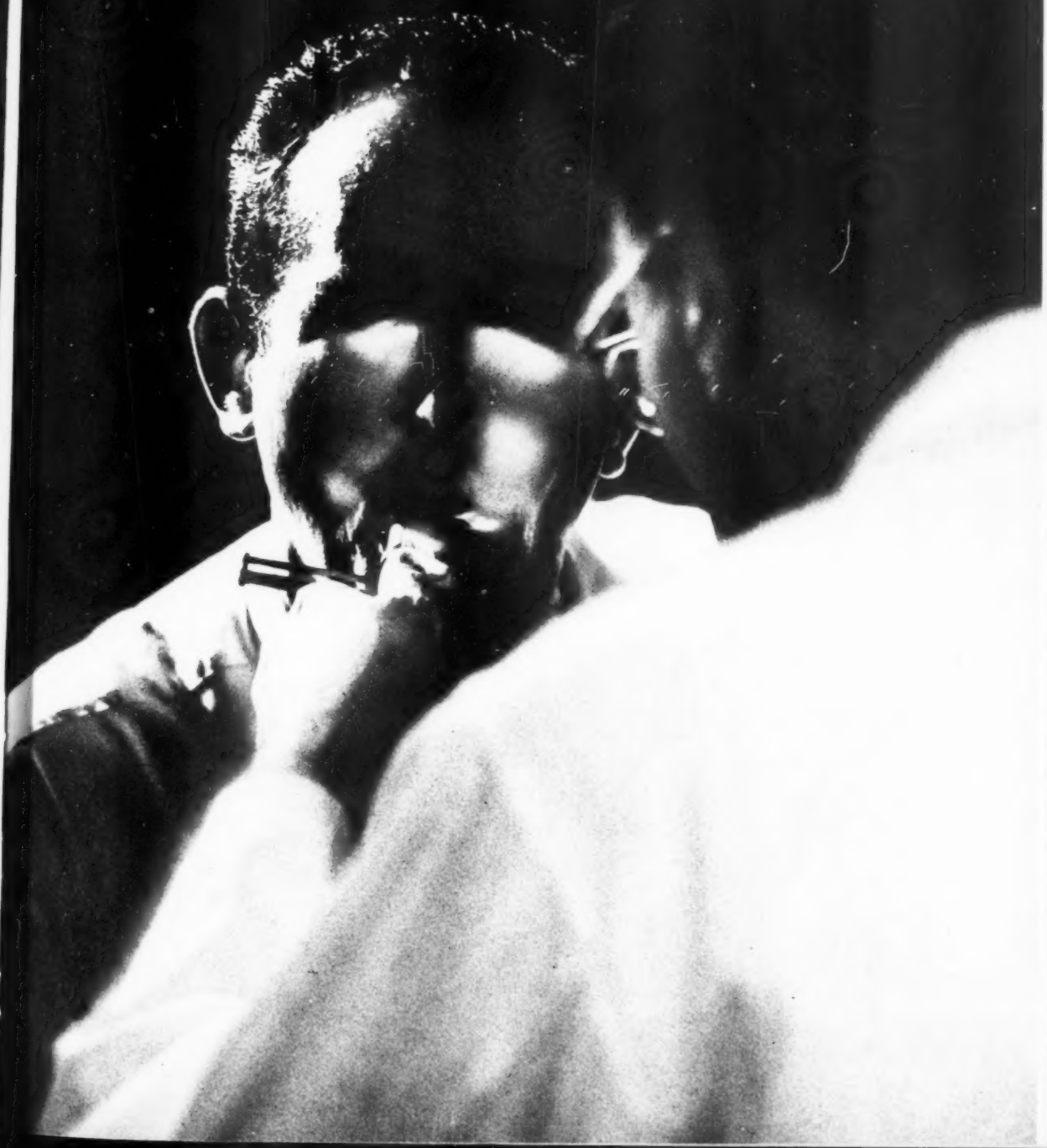
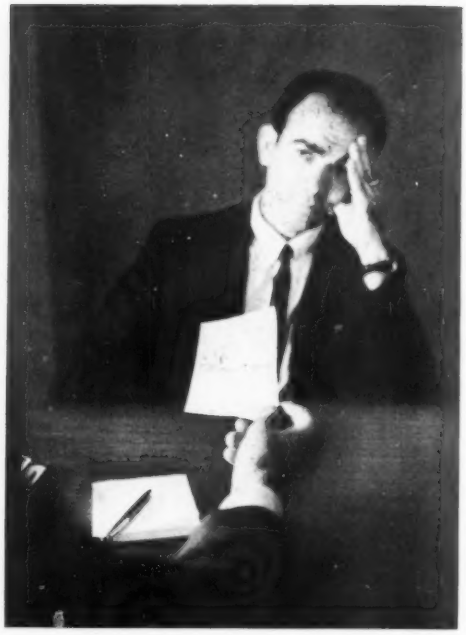


According to a recent report* on the effectiveness of Terramycin in 106 cases of upper respiratory tract infection: "The response in sinusitis was particularly gratifying, as both acute and chronic cases were controlled within an average of five days."

"It was the impression of the hospital staff that oxytetracycline [Terramycin] was not only better tolerated, but more effective than other antibiotics habitually used."

The results reported in this and many other studies confirm the vitality of Terramycin for broad-spectrum antibiotic therapy and demonstrate why —increasingly—the trend is to Terramycin.



## In brief

The dependability of Terramycin in daily practice is based on its broad range of antimicrobial effectiveness, excellent toleration, and low order of toxicity. As with other broad-spectrum antibiotics, overgrowth of nonsusceptible organisms may develop. If this occurs, discontinue the medication and institute appropriate specific therapy as indicated by susceptibility testing. Glossitis and allergic reactions to Terramycin are rare. Aluminum hydroxide gel may decrease antibiotic absorption and is contraindicated.

*More detailed professional information available on request.*

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*Jacques, A. A., and Fuchs, V. H.: J. Louisiana M. Soc. 113:200, May, 1961.

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## In Memorium

# Joseph Bank, M. D.

**January 25, 1898 - May 16, 1961**

**Joseph Bank, M.D.**

Joseph Bank will be missed by his many friends, patients and colleagues. It is fortunate that the Joseph Bank Medal was established in his honor during his lifetime. This award, established by the Maricopa County Medical Society, is to be given periodically to a physician for meritorious and outstanding community service. How fitting and characteristic this medal shall be.

Joe was born at the turn of the century in New York City. He received his M.D. degree from Jefferson Medical College in 1921. He became associated with Henry Bockus, professor of gastroenterology at the University of Pennsylvania Graduate School of Medicine and later was made assistant professor in the specialty at the graduate school.

In 1936, Joe came to Phoenix. He quickly became a leader in medical circles and community activities. He helped to establish the Blue Cross and Blue Shield plans here in Arizona. He was active in legislation to secure the passage of laws for pasteurization of milk and to provide for quarantine of contagious diseases. He helped to organize the United Jewish Appeal as well as the Zionist Organization

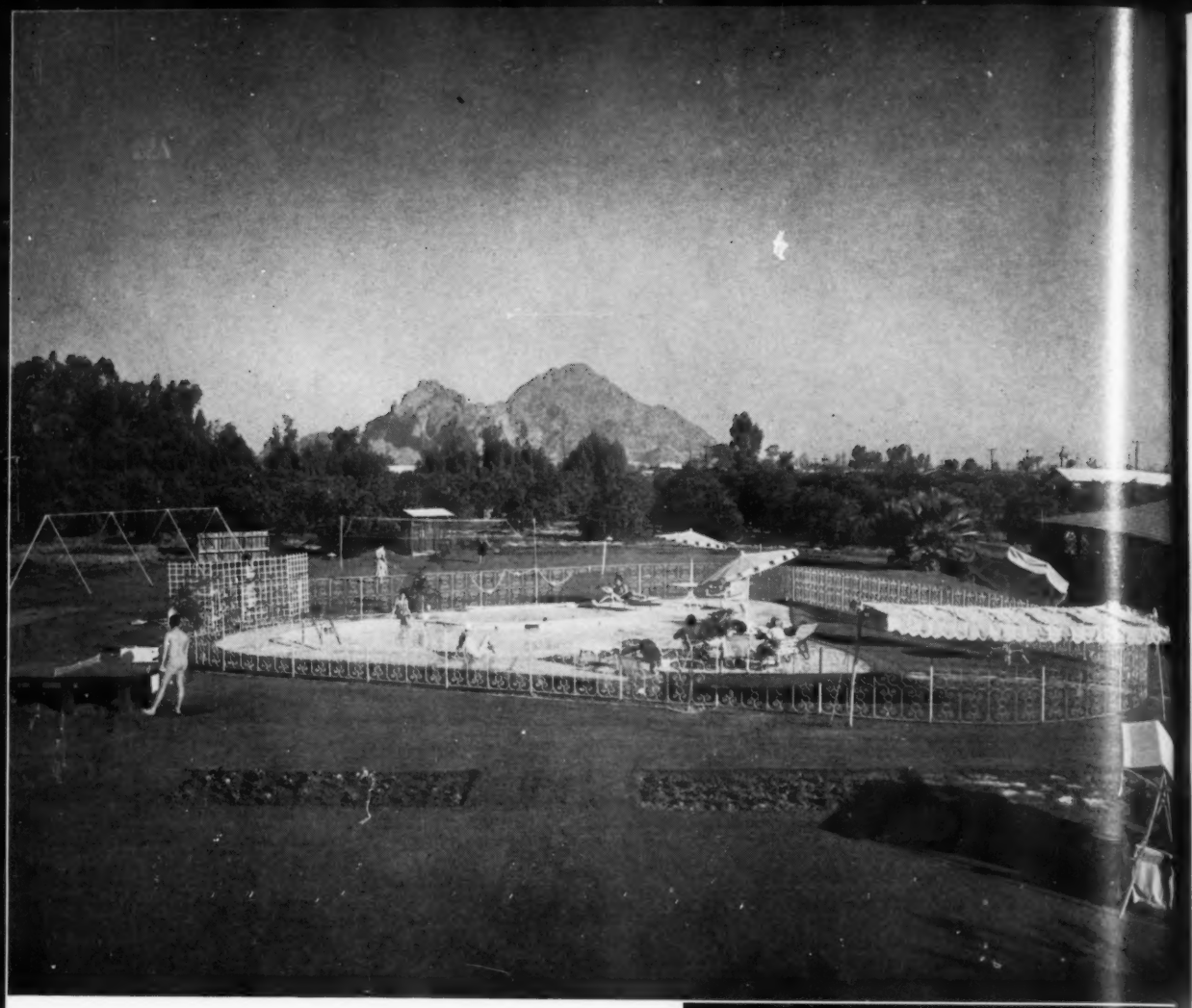
merica in Phoenix. He was a board member of Temple Beth Israel for many years.

During World War II he served at Beaumont General Hospital, where he headed the large medical section. He was separated from the service with the rank of lieutenant colonel.

Joe Bank was certified by the American Board of Internal Medicine in 1942. He was a member of the American College of Physicians and was president of the Southwestern Medical Association. We are particularly indebted to Joe for his calm and sage advice as a long-time active member of the Board of Directors of the Maricopa County Medical Society. Two years ago, he was named the American representative to the International Gastroenterology Association. He wrote many papers on the digestive tract and was author of the section on the examination of the abdomen in the Encyclopedia of Medicine.

The list of medical and civic accomplishments is long and worthy. But in addition, he was a kindly man, a good and just friend. He is survived by his wife, Ruth, and two sons, David and Daniel.

Jack Brooks, M.D.



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***Bright red, pleasant tasting, raspberry flavored syrup***

**Dosage:**

Children from 6 months to 1 year, 1/4 teaspoon; 1 to 3 years, 1/2 to 1 teaspoon; 3 to 6 years, 1 to 2 teaspoons; 6 to 12 years, 2 teaspoons. Every four to six hours as needed.

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## Topics of Current Medical Interest

# Barrow Neurological Institute*

Ground breaking ceremonies for the Barrow Neurological Institute took place on the grounds of St. Joseph's Hospital, Phoenix, Arizona, on January 14th, 1961. On this site the Institute will be constructed. (Fig. 1)

Gathered at these ceremonies were distinguished representatives of the State and Municipal Government, the two Universities located in Arizona, Religion, Hospital Administration, Organized Medicine, Local, State and National, Private Philanthropy and Public Interests. The remarks made by these representatives deserve recording, particularly as they refer to the entire project of constructing this neurological complex from the original idea to the soon to be realized goal of completion. The proceedings in entirety will be a permanent record in the History Archives of the Institute. Certain quotations of the speakers serve to construct a word picture of the enormity, complexity and importance of the project.

Mr. Charles A. Barrow, the major donor: "Over seven years ago we had a dream and now it has almost reached fulfillment. The future holds forth challenges to research." (Fig. 2)

Sister Mary Placida, Administrator of St. Joseph's Hospital, Phoenix, Arizona: "Research is usually not connected with a private hospital – grants are given to universities and schools of medicine for this purpose. We are going to prove that a private hospital can do the job in research just as well."

In effect, the Institute will be a memorial to the late William E. Barrow and to his daughter-in-law, Julia H. Barrow, the late wife of Charles A. Barrow. Mrs. Julia Barrow succumbed from a cerebral oligodendroglioma in 1959. She had been under the care of Dr. John R. Green from 1952 until the time of her death. Undoubtedly the association of the Barrow family with the present Director of the Institute, Dr. Green, served as the major impetus towards the beginning and advancement of the many carefully laid plans which will be culminated when the Institute becomes completed in 1962. Once in operation emphasis will be placed on research and education. Both public and private patients will be treated for neurological disorders.

The Right Reverend Msgr. Robert J. Donahue, V.F.: "Bless we beseech You, this ground and all the work which has gone before this moment by countless willing hearts and able hands."

Dr. Lindsay E. Beaton, President, Arizona Medical Association: "I think it is suitable that a physician stand here as the conductor of this celebration because he can perhaps most fittingly acknowledge the part that is played in modern medicine by persons other than physicians."

Here, in the invocation and opening remarks by the Chairman of Ceremonies who had been introduced by Mr. Thomas Chauncey, Executive Vice President of the Neurological Sciences Foundation, is recognition of the many individuals and of the many faceted problems encountered in this project.

The Hon. Paul Fannin, Governor of Arizona: "It is a great privilege for me to have the opportunity to participate in this ground breaking ceremony which brings this great addition to the science of medical arts here in our state, and the tremendous importance of this venture

*The material constituting the proceedings of the dedication was collected for permanent recording by Mrs. Roberta Hall, Chief Librarian of the Maricopa County Medical Society. The ceremonies were conducted most admirably by Dr. Lindsay Beaton, President, Arizona Medical Association and this article was compiled from the records of the dedication ceremonies for the present publication by Dr. Charles W. Elkins, Neurosurgery Editor, Arizona Medicine.

**Figure I**
**Proposed Barrow Neurological Institute**

**Figure II**
**Mr. Charles A. Barrow**

brought to reality should be realized by all the people of our state and throughout the nation."

The Honorable Sam Maridan, Mayor of Phoenix: "Our population is close to 450,000 people and we do need these new facilities."

Dr. Robert Nugent, Executive Vice President, University of Arizona, Tucson: "This is indeed an auspicious occasion which makes an important milestone in the history of Arizona and which is characteristic of the magnificent progress which our state has made, and is making, on so many fronts."

The two officials representing state and local government in Arizona and the representatives of the University of Arizona quite properly emphasized the continued growth of this portion of the Southwest and by logical succession this project will fit into its expanding economy and cultural growth. The actual initial plans for the Neurological Institute were formulated in December of 1954.

Rabbi Albert Plotkin, Jewish Churches: "Nothing can be greater in our time than to heal the wounds of a sick humanity."

Dr. Kermit Long, Phoenix Council of Churches: "It is no accident that the church has always been interested in the healing ministry, for whatever concerns the welfare of persons concerns the activity of the church. Disease is no respecter of persons. It strikes regardless of race, color, creed or status in life."

The Barrow Neurological Institute will be nonsecretarian — disease, it is realized, knows no religion. It crosses all lines — race, creed and color — and affects all people regardless of their material wealth or lack of it.

Mr. J. Frank Octigan, President of the Nuerological Sciences Foundation: "The functioning the Neurological Sciences Foundation is simple — it's a financial one. It is the fiscal right arm of the Institute."

Dr. Clarence Salsbury, Commissioner of the Arizona State Health Department: "I doubt if there is any other institution of this kind in Arizona for which Hill-Burton funds have been used up to the present time. But this is a very fine beginning for the use of such funds and for the use of such purposes."

The Neurological Sciences Foundation, which is made up of prominent Arizonans, was incorporated in 1959 and declared a tax exempt, nonprofit organization by the Department of Internal Revenue in 1960. This Foundation comprises the nucleus of many public spirited citizens who are supporting the Neurological Institute. Funds for the Institute were to a large extent donated by the Barrow Family. Federal matching funds (Hill-Burton) were obtained and also contributions were received from the National Institute of Health Research Facilities Division and from the Sisters of Mercy of St. Joseph's. The Neurological Sciences Foundation is committed to the funding of the research and educational programs of the Neurological Institute.

Dr. Robert Price, President of the Maricopa County Medical Society: "This is going to be a great blessing and a great stimulus to our community, for there are few such Institutes of Neurological Research in our country and indeed in the world."

Dr. Donald Polson, President of the Medical Staff of St. Joseph's Hospital: "Heretofore we have been dependent on other states for medical education and for medical progress, the results of research."

Dr. Loyal Davis, Chairman, Board of Regents, American College of Surgeons: "This contribution to the elevation of the care of the ill patient is a project which furthers the high ideals which our great College of Suregons has always proclaimed."

Once in operation, the Institute will serve on three levels: (1) a center for treatment of patients suffering from various organic disorders of the nervous system (2) as a center for basic research into the causes and treatment of nervous diseases (3) as a training center for neurologists, neurological surgeons and related research workers. The patient and his problems are rightfully the core of this integrated twentieth century approach.

Institute activities will be divided into five major divisions: neurology, neurosurgery, neuropathology, neuroradiology and experimental neurology. The problems of neurological patients cross the lines of the major cripplers and killers of mankind. These killing diseases include "strokes," cancer, brain disorders leading to death associated with childbirth, and accidents. Crippling neurological disorders include those which cause mental and emotional disorders, arteriosclerosis of the nervous system, epilepsy, Parkinsonism, cancer under treatment, cerebral palsy, multiple sclerosis and other degenerative

diseases of the nervous system, and muscular dystrophy. The proper diagnosis and treatment of these disorders is the major purpose of the Institute. The development of a team of clinicians and research workers who collaborate, stimulate and exchange ideas about the nervous system in health and disease is the basic organization of the Institute.

Dr. John R. Green, Director of the Institute: "The combination of an exploding population in Arizona, the humanitarian ideals of the Barrow family, outstanding public service of St. Joseph's Hospital, a dedicated medical staff, generous assistance from the medical profession, national and international consultants, architects (Mr. Ralph Morton and his associates) and The Neurological Sciences Foundation – these were the basic ingredients for the creation of the Barrow Neurological Institute.

"The challenge to measure up to this opportunity is recognized by all of us. On behalf of the clinical and the scientific staff, present and future, I wish to express our appreciation for the support that has been given. We wish to dedicate our combined efforts to make this an outstanding institution to treat neurological patients, to educate young men and women, and to do research in neurological sciences." (Fig. 3)

The ground breaking ceremonies for the Barrow Neurological Institute were concluded with the introduction of Mother Monica, representing the Mother House of the Sisters of Mercy and of those individuals already on the Staff of the Institute. These include:

Dr. Eduardo Eidelberg, M.D., at the present time Associate Research Professor of Anatomy at the University of California in Los Angeles, who will be Chairman of Experimental Neurology at this Institute.

Dr. James W. Kernohan, M.D., presently Senior Consultant in Pathology in the Mayo Clinic and Foundation who will be Chairman of Neuro-Pathology at the Institute.

Other members of the present medical staff who were introduced were Dr. Harry F. Steelman, Dr. Hal W. Pittman, Dr. Betty Clements, Dr. John A. Eisenbeiss, Dr. William Helme, Dr. E. Thornton Pfeil, Dr. George Hoffman, Dr. John Schramel, Dr. Kenneth Rew, Dr. James Riordan, Dr. Robert Flynn, Dr. John Hancock, Dr. Onie Williams, Dr. Lorel Stapeley, Dr. Frank Mann, Dr. George B. Kent, Jr., Dr. Heinz F. Hoenecke and Dr. Richard E. McGovern.

**Figure III**
**John R. Green, M.D., Director**
**Barrow Neurological Institute**

Dr. Lindsay E. Beaton: "In the literature of the ancient and of the Renaissance, the man who was a patron deserved an equal place with the artist or the scientist whose works he made possible."

Mr. Charles A. Barrow, together with other members of the family, has contributed well over a million dollars to make possible the construction of one of the most modern complete neurological units of its kind in the world. May the Institute grow and prosper and from the minds of its workers arise the solution of many problems which at the present time seem perplexing. By coordination of activities and integration of ideas in this type of institution will these problems be solved.

Msgr. Donahue: "Grant, we beseech Thee, that what we are starting to build for the glory of Thy name, may by the ever present aid of Thy fatherly wisdom be brought to completion."

Charles W. Elkins, M.D.

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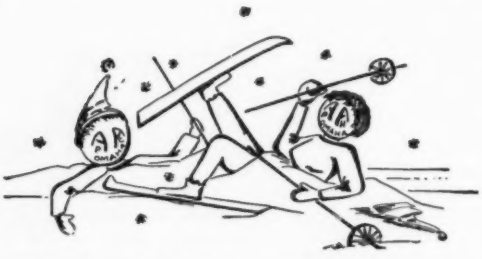

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Reprints

# Cancer Chemotherapeutic Agents

David A. Karnofsky, M.D.

## SPECIFIC AGENTS USED IN CANCER CHEMOTHERAPY

| | AGENTS | Principal Route of Administration | Usual Dose | Acute Toxic Signs | Major Late Toxic Manifestations |
|---|---|---|---|---|---|
| STEROID COMPOUNDS AND ACTH | **Androgen** | | | | |
| | Testosterone propionate | I.M. | 50-100 mg. 3 x weekly | None | Fluid retention, masculinization. |
| | Fluoxymesterone (Halotestin®) | Oral | 10-20 mg. daily | | |
| | **Estrogen** | | | | |
| | Diethylstilbestrol | Oral | 1-5 mg. 3 x daily | Occasional | |
| | Ethinyl estradiol (Estinyl®) | Oral | 0.1-1.0 mg. 3 x daily | N. & V* | Fluid retention, feminization, uterine bleeding. |
| | **Progesterone** | | | | |
| | Hydroxyprogesterone caproate (Delalutin®) | I.M. | 500 mg. 3 x weekly | None | |
| | **Adrenal Cortical Compounds** | | | | |
| | Cortisone acetate | Oral | 50-300 mg. daily | | |
| | Hydrocortisone acetate | Oral | 50-200 mg. daily | None | Fluid retention, hypertension, diabetes, increased susceptibility to infection. |
| | Prednisone (Meticorten®) | Oral | 20-100 mg. daily | | |
| | **Adrenocorticotropic Hormone** (ACTH) | I.V.<br>I.M. | 25-50 mg. by continuous infusion<br>10-20 mg. every 3 hrs. | None | |
| RADIOACTIVE ISOTOPES | **Iodine** ($I^{131}$) | Oral<br>I.V. | 100-200 mc. | None | Myxedema, bone marrow depression, renal damage. |
| | **Phosphrous** ($P^{32}$) | Oral<br>I.V. | 3-7 mc. | None | Bone marrow depression. |
| | **Gold** ($Au^{198}$) | Intrapleur.<br>Intrabd. | 75 mc.<br>75 mc. | None | Bone marrow depression. |
| POLYFUNCTIONAL ALKYATING AGENTS | **Methylbis (B-Chloroethyl) Amine HCl** (HN2, Mustargen®) | I.V. | 0.4 mg./kg. Single or Divided Doses | N. & V. | |
| | Chlorambucil (Leukeran®) | Oral | 0.1-0.2 mg./kg./day | None | Therapeutic doses, moderately depress peripheral blood cell count; excessive doses cause severe bone marrow depression with leukopenia, thrombocytopenia, and bleeding. Maximum toxicity may occur two or three weeks after last dose. Dosage, therefore, must be carefully controlled. Alopecia occurs occasionally with cyclophosphamide. |
| | Cyclophosphamide (Endoxan, Cytoxan®) | I.V. | 3.5-5.0 mg./kg./day x 10 (40-60 mg./kg. Single dose) | N. & V. | |
| | | Oral | No Estab. Dose | | |
| | **Triethylene Melamine** (TEM) | I.V. | 0.04 mg./kg. x 3 | Occasional | |
| | | Oral | 20-40 mg. in 1 mo. | N. & V. | |
| | Triethylenethiophosphoramide (TSPA, ThioTEPA®) | Oral<br>I.V. | 5-10 mg./day<br>0.2 mg./kg. x 5 | None | |
| | **1,4-dimethanesulfonyloxybutane** (Busulfan, Myleran®) | Oral | 2-8 mg./day<br>150-250 mg./course | None | |
| ANTIMETABOLITIES | **4-Amino-$N^{10}$-methylpteroylglutamic acid** (Amethopterin, Methotrexate®) | Oral | 2.5-5.0 mg./day | None | Oral and digestive tract ulcerations; bone marrow depression with leukopenia, thrombocytopenia, and bleeding. |
| | 4-Aminopteroylglutamic acid (Aminopterin) | Oral | 0.25-1.0 mg./day | | |
| | **6-Mercaptopurine** (6-MP, Purinethol®) | Oral | 2.5 mg./kg./day | None | Therapeutic doses usually well tolerated; excessive doses cause bone marrow depression. |
| | 6-Thioguanine (6-TG) | Oral | 2.5 mg./kg./day | | |
| | **5-Fluorouracil** (5-FU) | I.V. | 15 mg./kg./day x 3-5 | None | Stomatitis, nausea, GI injury, bone marrow depression. |
| MISC. DRUGS | **Urethane** | Oral | 2-4 gm. daily | N. & V. | Bone marrow depression. |
| | **Potassium arsenite** (Fowler's solution) | Oral | 0.2-1.0 cc. daily | None | Diarrhea, vomiting, skin eruptions. |
| | **Actinomycin D** | I.V. | 15 gamma/kg./day x 5 | N. & V. | Stomatitis, GI disturbances, alopecia, bone marrow depression. |
| | **Demecolcin** | Oral | 5-8 mg./day | None | Alopecia, bone marrow depression. |
| | **o-p,'DDD** | Oral | 2-10 gm./day | N. & V. | Skin eruptions, diarrhea, mental depression, muscle tremors. |

Reprinted by permission from the March-April 1961 issue of CA, a Cancer Journal for Clinicians published by the American Cancer Society, Inc.

## NEOPLASTIC DISEASES RESPONDING TO CHEMOTHERAPY

| DIAGNOSIS | Polyfunctional Alkylating Agents | Antimetabolities | Radioactive Isotopes | Steroid Hormones | Miscellaneous Drugs | RESULTS |
|---|---|---|---|---|---|---|
| **Leukemia** Acute, Children | | 6-MP Amethopterin | | Adrenal Cortical Hormones | | 70% bone marrow improvement; 50% patients live one year or longer. |
| Acute, Adults | | 6-MP Amethopterin | | Adrenal Cortical Hormones | | 15-25% improved for several months or longer. |
| Chronic Myelocytic | Myleran® HN2 | 6-MP | $P^{32}$ | | Demecolcin Urethane Fowler's solution | Patients maintained in good condition during major portion of disease; life occasionally prolonged. |
| Chronic Lymphatic | Chlorambucil TEM | | $P^{32}$ | Adrenal Cortical Hormones | | Patients maintained in good condition during major portion of disease; life occasionally prolonged. |
| **Hodgkin's Disease** | Chlorambucil HN2 TEM | | | Adrenal Cortical Hormones | | Occasional favorable response, but no definite prolongation of life. |
| **Lymphosarcoma** | Chlorambucil HN2 TEM | | | Adrenal Cortical Hormones | | Occasional favorable response, but no definite prolongation of life. |
| **Multiple Myeloma** | | | $P^{32}$ $I^{131}$ | Adrenal Cortical Hormones | Urethane | Symptomatic relief in about 50% of cases, and objective hematological improvement in 15%. |
| **Polycythemia Vera** | Myleran® TEM HN2 | | $P^{32}$ | | | Prolonged clinical remissions, particularly with $P^{32}$. |
| **Carcinoma of Lung** | HN2 TEM | | | | | Brief improvement in about 50% of cases. |
| **Carcinoma of Ovary** | TEM HN2 | 5-FU | | | | 30 to 50% of cases improved for one to three months, sometimes longer. |
| **Carcinoma of Thyroid** | | | $I^{131}$ | | | Frequently marked improvement in properly selected cases. |
| **Carcinoma of Breast** | TEM HN2 | | | Estrogens Androgens Adrenal Cortical Hormones | | 20 to 50% improved by hormonal therapy; life may be prolonged in some cases. |
| **Carcinoma of Endometrium** | | | | Delalutin | | 35% regression reported. |
| **Carcinoma of Prostate** | | | | Estrogens | | 80% of cases respond to hormonal therapy; definite prolongation of life. |
| **Wilms' Tumor** | HN2 | | | | Actinomycin D | Temporary regression with 30% pulmonary metastases. |
| **Choriocarcinoma,** Female | HN2 | Amethopterin | | | | 80% respond, of whom 30% show "permanent" regression. |
| **Carcinoma of Colon** | | 5-FU | | | | 15% respond for several months. |
| **Carcinoma of Adrenal** | | | | | o,p'DDD | Tumor regression and decrease in hyperadrenocorticism in selected cases. |
| **Carcinoma of Testis** | Chlorambucil* | Amethopterin* | | | Actinomycin D* | 35% of patients show a favorable and sometimes prolonged response. |
| Miscellaneous Carcinomas and Sarcomas | HN2 TEM Chlorambucil Cyclophosphamide | | | Adrenal Cortical Hormones | | In rare instances, favorable responses occur. |

*Given in Combination

## REGIONAL CANCER CHEMOTHERAPY

| | | | | |
|---|---|---|---|---|
| **Carcinoma in Facial Areas** | | Amethopterin + Citrovorum Factor (Intraarterial infusion) | | Favorable response of tumors supplied by external carotid artery. |
| **Tumors of the Extremities** | HN2 (extra-corporeal perfusion) | | | Response in selected cases. |
| **Pleural, Pericardial and Abdominal Effusions** | HN2 (local instillation into appropriate cavity) | | $Au^{198}$ $CrP^{32}O^{4}$ (local instillation of drug into appropriate cavity) | About 25 to 50% of patients respond |
| Leukemic Involvement Central Nervous System | | Amethropterin (intrathecal injection) | | About 80% of children with CNS involvement respond temporarily. |

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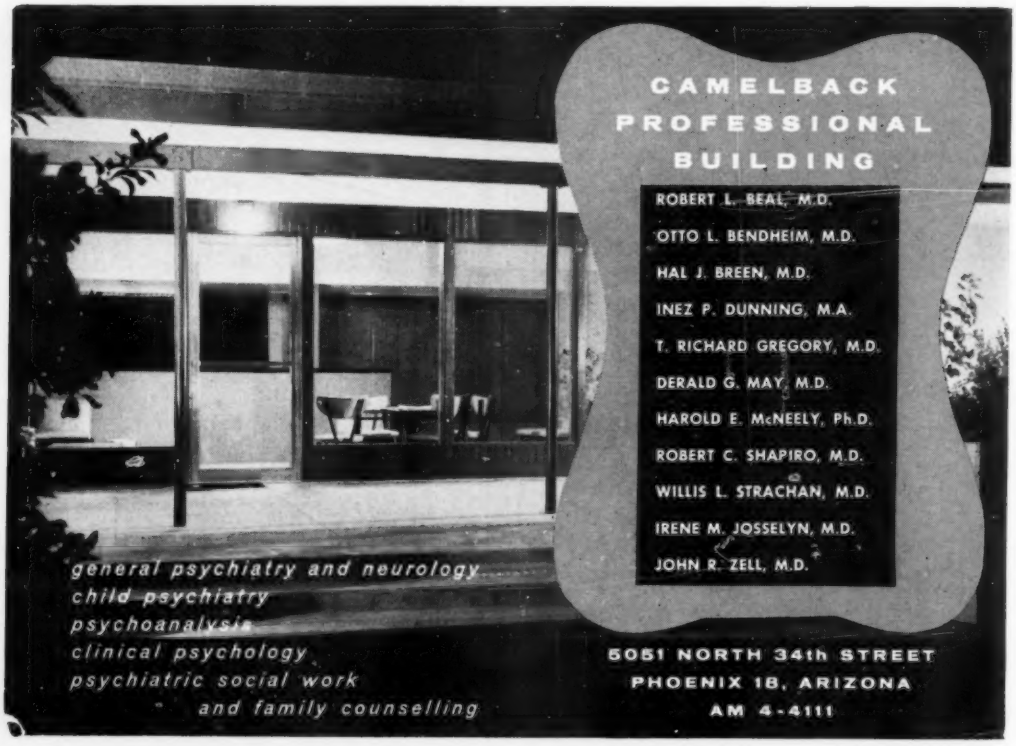

## Future Medical Meetings and Postgraduate Education

# REGIONAL MEETINGS
# Winter & Spring, 1961-62

December 26-31, 1961
128th Meeting, American Association for the Advancement of Science
Denver, Colorado

February 20-23, 1962
Colorado State Medical Society
Midwinter Clinical Session
Denver, Colorado

March 1-3, 1962
University of Utah College of Medicine
Postgraduate Course — Obstetrics
Salt Lake City, Utah

March 15-17, 1962
Tenth Annual Cancer Seminar
Arizona Division
American Cancer Society
Phoenix, Arizona

March 26-June 7, 1962
Colorado University Medical School
Postgraduate Course — Surgical Anatomy
Denver, Colorado

April 2-5, 1962
Southwestern Surgical Congress
Albuquerque, New Mexico

April 6-13, 1962
American Academy General Practice
Annual Meeting
Las Vegas, Nevada

April 24-28, 1962
Arizona Medical Association
Scottsdale, Arizona

April 27-28, 1962
Western Colorado Spring Clinic
Grand Junction, Colorado

May 9-11, 1962
New Mexico Medical Society
Annual Meeting
Hobbs, New Mexico

June 27-30, 1962
Idaho State Medical Association
Sun Valley, Idaho

### AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

Annual Meeting
December 29-30, 1961
Hilton Hotel
Denver, Colorado

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### MAN AND CIVILIZATION: CONTROL OF THE MIND — — II

The University of California School of Medicine and the Department of Continuing Education in Medicine and Health Sciences announces its second symposium, "Man and Civilization: Control of the Mind — II." This international symposium will be held at the University of California Medical Center, San Francisco, California, January 26-29, 1962.

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### INTERNATIONAL MEDICAL-LEGAL SOCIETY

Announces its
Second Postgraduate Seminar
February 19-23, 1962
Honolulu, Hawaii

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### THE NEW ORLEANS GRADUATE MEDICAL ASSEMBLY

The twenty-fifth annual meeting of the New Orleans Graduate Medical Assembly will be held March 12-15, 1962 at The Roosevelt Hotel. A clinical tour to the Mediterranean follows the New Orleans Meeting.

## ARIZONA HEART ASSOCIATION
### Fifth Annual Cardiac Symposium
### January 26-27, 1962
**ARIZONA BILTMORE HOTEL**
**Phoenix, Arizona**

FRIDAY, JANUARY 26, 1962

| | |
|---|---|
| 8:00- 9:00 a.m. | Registration – Lobby Entrance |
| 9:00- a.m | Greeting by Dr. Shaw McDaniel, Phoenix, President, Arizona Heart Association |
| 9:15- 9:55 a.m. | External Cardiac Massage and Defibrillation<br>Dr. Alfred Blalock, Baltimore, Maryland |
| 9:55-10:35 a.m. | Changing Concepts of Heart Failure<br>Dr. James V. Warren, Columbus, Ohio |
| 10:35-10:50 a.m. | Intermission – Visit Exhibits |
| 10:50-11:30 a.m. | Effects of Potassium-Glucose-Insulin Treatment on the Electrocardiographic Signs of Myocardial Infarction |
| 11:35-12:15 p.m. | Obstruction and Regurgitation – The Physician and Physicist<br>Dr. Hans H. Hecht, Salt Lake City, Utah |
| 12:30- 2:00 p.m. | Luncheon at the Poolside |
| 2:00- 2:40 p.m. | The Long Term Management of Coronary Artery<br>Dr. James V. Warren, Columbus, Ohio |
| 2:40- 3:20 p.m. | Recurrent Problems in Atrial Fibrillation<br>Dr. Hans H. Hecht, Salt Lake City, Utah |
| 3:20- 3:35 p.m. | Intermission |
| 3:35- 4:30 p.m. | Panel Discussion of Current Cardiovascular Problems<br>Dr. Robert N. Class and Dr. Earl J. Baker, Moderators |

SATURDAY, JANUARY 27, 1962

| | |
|---|---|
| 8:30- 9:30 a.m. | Registration continued – Lobby |
| 9:30- a.m. | Greeting by Dr. Harold J. Rowe, President-elect, Arizona Heart Association |
| 9:45-10:25 a.m. | A new Classification of Myocardial Infarction<br>Dr. Demetrio Sodi Pallares, Mexico, D.F. |
| 10:25-11:05 a.m. | Recent Developments in our Knowledge of Syncope<br>Dr. James V. Warren, Columbus, Ohio |
| 11:05-11:20 a.m. | Intermission |
| 11:20-12:00 a.m. | Comparative Studies on Altitude Physiology – An Everyday Lesson<br>Dr. Hans H. Hecht, Salt Lake City, Utah |
| 12:00- 2:00 p.m. | Luncheon |
| 2:00- 2:40 p.m. | Bilateral Bundle Branch Block – Dr. Demetrio Sodi Pallares, Mexico, D.F. |
| 2:40- 3:20 p.m. | Recent Advances in Cardiovascular Surgery<br>Dr. Alfred Blalock, Baltimore, Maryland |
| 3:20- 3:35 p.m. | Intermission |
| 3:35- 4:30 p.m. | Panel Discussion of Current Cardiovascular Problems<br>Dr. George W. King and Dr. Arthur R. Nelson, Moderators |

## The Dallas Southern Clinical Society
Spring Clinical Conference
March 19-21, 1962
Statler Hilton Hotel
Dallas, Texas

## 10th ANNUAL CANCER SEMINAR
of the Arizona Division
AMERICAN CANCER SOCIETY
in conjunction with
National Science Writers Seminar
March 15-17, 1962 – Phoenix, Arizona

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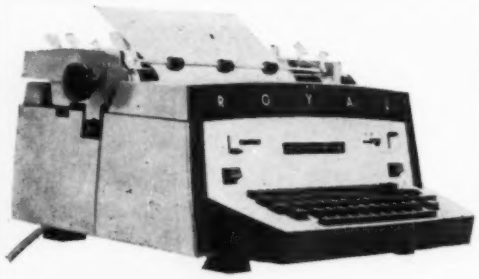


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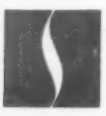

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